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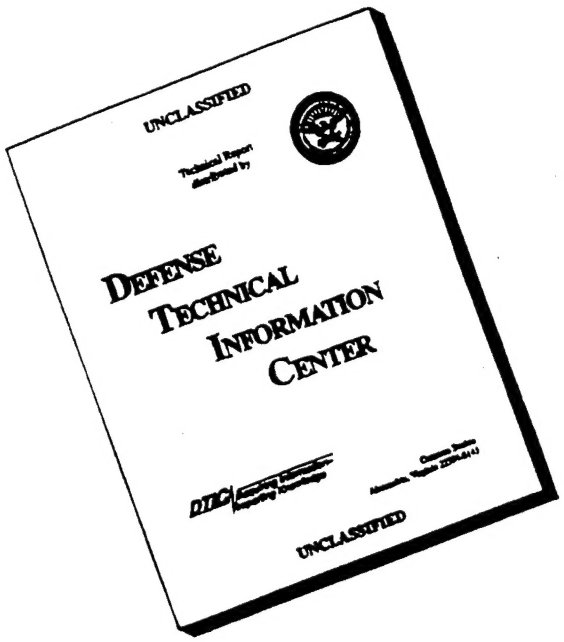

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13. ABSTRACT *(Maximum 200 words)*

Work to optimize the appearance of digitized film mammography and digital mammography using storage phosphor technology is nearly complete. The attached report and its appendices indicate that digitized film mammography (digitized at 100 micron pixel size) is insufficient for clinical interpretation with soft copy display. Hard copy display is still insufficient, however, we are planning tests of a newer method for hard copy display during the coming (final) year of the project. Digital mammography using storage phosphor methods has been optimized and an ROC analysis of this method using our current data set of approximately 30 proven cancer cases and a matched number of benign cases is about to begin. This ROC study will compare matched conventional and digital images using six radiologists. Each of the cancer and benign finding cases is pathologically proven. We are also exploring special image processing methods for the radiodense breast and these are discussed in this report.

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Army Report 1996
Clinical Optimization of Current Digital Mammography Systems

Introduction

Army grant DAMD17-93-J-3008 was initiated in December 1992 for completion in December 1995. This completion data has not been met because of equipment and software problems caused by outside suppliers. We have requested a one year, no cost extension by which time the project should be completed.

The original purpose of this project was to test existing methods for digital mammography. We discovered in this process that the methods current in 1992 were not sufficient for digital mammography and that we needed to encourage and cajole manufacturers into modifying and/or making the devices we needed. This resulted in delays in the progress of the project. In this process we have had to work directly with Fuji Photo Film Corporation in the U.S. and with their Development facilities in Japan, with DBA Inc. in Florida, with Analogic Corporation in Peabody, MA, with 3M in St. Paul, MN, with Polaroid in Newton, MA, as well as develop our own software. One of our outside suppliers was unable to meet equipment specifications for the film digitizer (this supplier was replaced). Another supplier delayed the delivery of equipment for six months and the software provided needed to be rewritten to eliminate bugs that resulted in equipment crashes (with a six month additional delay). We also found that a key component of printer server software that we needed did not exist in the commercial market. We have worked with our current supplier over the last two years and now have a successful print server for quality mammographic images. All of the hardware needs for this project are to be available as of mid-February 1996.

The purpose of this project is to determine whether or not digital mammography is feasible with existing equipment either by using digitized film or by using direct digital acquisition using storage phosphor technology. The brief answer is that it was not feasible with the equipment available at the initiation of the grant. There has been substantial development over the past three years and we believe our data from the ROC analysis that we are about to begin will show that digital mammography is feasible using direct acquisition, but not using digitized film. This project has, based on our findings and advice, we believe, guided manufacturers to develop the necessary tools.

Digitized Film Mammography

The evaluation of digitized film required a process of quality control of the digitization equipment and display equipment that has been completed and a preclinical trial of proven cases, the first phase of which has been completed. This first phase demonstrated that digitized film mammography at 100 micron pixel size was considered clearly inferior to the original films by each of the five radiologists who reviewed its display on a workstation and that this lower quality would decrease the detectability of breast cancer. Digitization of a small sample of two different film screen systems of different latitude demonstrated that they both were of sufficient contrast that information close to the skin line and within the dense portions of the breast could not be adequately demonstrated with either system. The characteristic curves of these two screen film systems are shown in Appendix 1. Initial laser prints of 50 micron digitized film mammography in June 1993, were of poor quality because of the lack of an appropriate print server with correct image processing. An improved print server system designed with the PI's help was partially installed in November 1995 and full software for this should be available by mid-February 1996. At

this point we will do a comparative study using a random sample from the 130 proven clinical cases we have digitized and stored in electronic form and compare the results to the original film screen mammograms and the findings at biopsy.

A full report on the evaluation of digitized film mammography at 100 microns with soft copy interpretation compared to the original screen-film mammogram is attached as Appendix 2. In this evaluation we used 25 cancer cases and 25 benign cases that had biopsy for suspicion of cancer. In almost all cases the radiologists preferred the original mammogram to the soft copy 100 micron digitized mammogram for microcalcifications. The original mammogram also was preferred for most cases of masses, though there were a few more cases in which the two methods were considered equivalent.

Storage Phosphor Digital Mammography

The evaluation of direct digital mammography using storage phosphor technology required machine and software optimization. In order to accomplish this it was necessary to perform a long optimization procedure that has been detailed in the two prior annual summaries. Briefly, a multivariate analysis was performed using response surface experimental design methods to define the optimal exposure and image processing factors for digital mammography. The results of this, summarized below and in the attached paper (Appendix 3) demonstrated that storage phosphor digital mammography using a 100 micron pixel and proper exposure and image processing optimization could result in images of standard mammographic phantoms that showed objects equal in size or smaller than those shown in standard screen film mammography and that the resulting images were highly pleasing to viewers. Additionally, we found that digital mammography may prove to be especially useful for the detection of cancer in the radiodense breast. These findings are detailed below.

TABLE OF SMALLEST OBJECT SEEN

Test Object	Screen Film	100 micron phosphor	50 micron CCD
CDMAM	130. 100 at 5x mag	100 at 1 micron thick	100 at 0.8 microns thick
CIRS Detail	240	160	160
RMI 156	240 (3/6)	240 (3/6))	240 (3/6)
Steel Fleck	100	50 (noisy, high contrast)	100
CIRS Half Round	160	160	160

This table demonstrates that in two of the test objects, the 100 micron storage phosphor allowed detection of smaller objects than screen film mammography and that in the other two standard geometric test objects, that it provided the same object visibility as screen film mammography. The steel fleck phantom is a home-made system and showed that if a 50 micron object were of sufficient radiodensity, it could be identified on a 100 micron system, though it would measure larger than its true size. (From Freedman, 1995 A)

A comparison of a 50 micron digital spot device based on CCD technology and a 100 micron whole breast system using storage phosphor technology was performed and reported in February 1995, and demonstrated that the 50 micron system provided higher contrast, but did not allow smaller objects to be detected and that the 50 micron system needed 1.5 to 3 times the exposure of the 100 micron system. (Appendix 4) In the above table, the improved contrast from the 50 micron system is demonstrated for the CDMAM phantom for which a thinner object could be seen with the 50 as compared to the 100 micron system. Both were superior in resolution to screen film mammography. These results were specific to the devices tested and cannot be generalized,however.

Collaborative Relationship with Army Medical Centers

Our original intention of working with Madigan and Brooke Army Medical Centers has been modified so that we are now working with Colonel Robert Shah, MD at Brooke Army Medical Center and Colonel Ted Raia's designee, (currently Major Robert Leckie, MD, and starting July 1, Major Morgan Williamson, MD) at Walter Reed Army Medical Center. We also consult with and obtain advice from by Major Donald Smith, MD at Madigan.

Methods

Clinical Case Series

We have been collecting a set of cases in which we have in each case the original screen film mammogram, the storage phosphor 100 micron direct digital mammogram obtained on the latest update of equipment and software, and the biopsy specimen radiograph. We currently have over 130 cases containing more than 30 proven cancers. The data for the direct digital mammograms is stored electronically and each of the original screen film mammograms has been digitized and is available in 50 micron and 100 micron formats. As of November 1995, we have sufficient cases of adequate quality to perform an ROC study. Because of an important update in software that resulted in improved digital mammography acquisition, an earlier dataset was not used; the current dataset has been collected since March 1995. We have delayed starting our ROC study because we expect to have a better laser film printer for the digital images available late in January 1996.

We have also digitized 100 cases in which we can compare wider and narrower latitude films. The Prior film system was the Dupont Mammography screen film system. The newer higher contrast system is the Fuji IM Fine mammographic system and has moderately higher contrast.

Digitized Film Methodology

Our initial choice of film digitizer (DBA, Inc.) proved unstable and despite many attempts by the manufacturer to improve the product, remained unstable. Eventually, we decided that the system would not be able to provide the quality we needed and therefore decided that it was unsuitable. In 1995, we switched to the Lumisys 50/100 micron system. We have digitized approximately 2000 mammogram films with this system. The system still shows intermittent instability, but is adequate for our experiments.

Digitized Film Mammography Display

We have developed display parameters for the soft copy display of digitized film mammograms on the Vicom display system. This Sun computer based system using Megascan monitors provides sufficient flexibility to allow us to test soft copy display. We have performed a reader comparison study in which 25 cancer images, 25 benign biopsy cases and 50 normal images were compared by 5 radiologists who evaluated the image preference looking at the visibility of microcalcifications, masses, and asymmetric densities on the original screen film mammogram and on the soft copy display. The full report of this is attached as Appendix 2. The radiologists were allowed to adjust the window level and width on the displayed images. All 5 radiologists expressed strong preference of the hard copy display for microcalcifications. In some cases the microcalcifications could not be seen on the soft copy display and in some cases dust and pick artifacts appeared on the soft copy display with an appearance that could not be distinguished from the appearance of

microcalcifications, whereas on the hard copy display they could be easily determined to represent dust or pick artifacts.

So far we have assessed only 100 micron pixel digitized film images. We will evaluate a smaller sample of 50 micron digitized film images in the near future. We do not have a clinically usable method for the display of 50 micron digitized film images on soft copy displays since the pixel size exceeds that of available monitors. Thus, one ends up looking at images in segments--1/4 of the image displayed at a time. This, therefore, would not be clinically practical. Our original concept was that one could assess the image with the pixels combined to produce 100 micron pixel size and zoom into the full dataset when a suspicious region was found. What we have found is that we cannot identify many of the regions containing suspect calcifications on the 2K matrix-100 micron pixel images and therefore would not know where to zoom the image. We consider zooming the entire image impractical for clinical use. We are unaware of any 4K display with sufficient luminance for clinical radiography. This is described more fully in Appendix 2.

Digitized Film Mammography: Hard Copy Display

Our first hard copy display of digitized film mammography was in June 1993. The initial system did not provide adequate control of contrast and unsharp masking. It was clear from this initial work that the image processing capabilities of our available print server system were not sufficient for adequate display of mammography. Over the past 15 months we have been working with a supplier of print servers (Analogic Corp.) to have them build into their system adequate capabilities for us to obtain proper control of the digitized film mammography printing to assure high quality images with our existing laser printers. We are still waiting for one final piece of hardware/software for this process which we believe will be available by mid February 1996. At present, we do not consider the hard copy images of digitized film mammography adequate for clinical diagnosis. We do not know if this is caused by the digitization process or by the printing process, since we know that the printing process is still not optimal.

Direct Digital Method

Images are currently acquired using Fuji HR-V imaging plates and a Fuji 9000 Computed Radiography system. Based on problems we identified during beta testing of this system, it was modified and appears adequate for digital mammography. Images are automatically processed using Fuji's standard parameters and the unprocessed data is then stored on the Fuji 954 workstation. We reprocess the image data sets to meet our optimized image processing standards. The image data sets are then transferred for permanent storage to a Fuji optical disk drive to provide for long term optical disk storage. This image data can be transferred through an Analogic DASM to an Analogic experimental workstation which serves both as a print server and a method of transferring the images over our internal network. The Analogic print server can (as recently developed) mimic the Fuji print parameters (except for DRC) printing to a 3M laser printer. It can also send processed images for printing as Tiff files to other printers. As of November 1995, the system is also capable of sending processed images to our Vicom workstation for soft copy viewing. Tests of the accuracy of soft copy reading will be performed in 1996.

Image Processing for the Direct Digital system can be performed using the standard Fuji Parameter settings. We have also found it of value to use specially designed dynamic range control curves for printing digital mammography in the radiodense breast. Our previous Annual Reports to the Army documented the procedures used to optimize image appearance.

Direct Digital Images: Hard Copy Display

We have found that the standard Fuji laser printer supplied with the original Fuji 9000 was acceptable, but less than optimal. We have printed some of these images on a Polaroid Helios Printer and other images on a 3M 969 Laser Printer and have found the image quality of these prints superior to that of the Fuji FL-IM 3543 laser printer. The main reason for this is that when the images are magnified with a hand lens, the scanning lines from the Fuji FL-IM 3543 laser printer are sufficiently wide that they interfere with the detection of microcalcifications. The other two printers have less apparent scan lines (3M) or inapparent scan lines (Polaroid) resulting in images that radiologists prefer. We have on order Fuji's latest printer, the FL-IM D, to determine whether that system is better. At this time, we believe that the Polaroid Helios Printer will prove to be optimal, but we do not currently have funds to purchase this printer and therefore must work through Polaroid's generosity and willingness to print these images for us in their research laboratory. Polaroid informed us in February 1996 of their intention to place a Helios Printer at Georgetown to expedite the testing of this printing system.

Direct Digital Images: Viewer Acceptance of Hard Copy Display

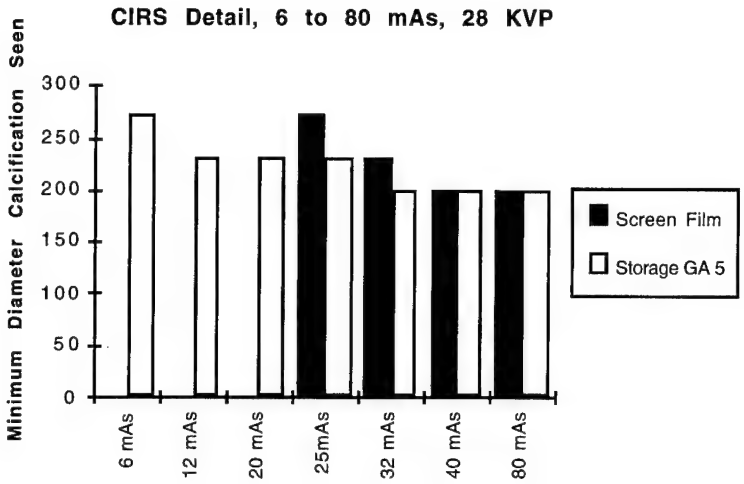
We have displayed comparison images from the Fuji computed radiography digital system and conventional screen film images in several meetings. The acceptability of these images has been considered high by many of those viewing the images at meetings. At the RSNA Annual Meeting, 1994, we demonstrated with a backlit display the original screen film images and CR digital images of the standard breast geometric test objects, three cancers (5, 6, and 15 mm) manifested by microcalcifications, one 8mm cancer manifested by spiculated mass, and two microcalcification cases that on biopsy showed benign findings. We provided magnifying glasses and asked those who wished to indicate which images they preferred. Ninety-four percent of those who responded preferred the digital images of the test objects, 83% preferred the clinical microcalcification cases, and 57% preferred the one mass case we showed. We have shown a similar exhibit at the American Roentgen Ray Meeting in May 1995, where the exhibit received a bronze medal. The direct digital images appear to be acceptable to many of those viewing them.

ROC Study of Direct Digital Images

This study has been delayed because improvements of hardware and software that occurred in March 1995 were of sufficient magnitude that we decided not to use our prior data, but only the newest data. We have, as of December 1995, more than 130 cases containing 30 cancers, a sufficient number to perform an ROC study. We will be performing this early in 1996. We have been delaying this ROC study briefly while we await a better laser printer. This is expected to be available early in 1996.

Direct Digital Mammography and the Radiodense Breast

In 1993, we determined that the wider exposure latitude of the storage phosphor plate system did indeed allow the recording of useful information in mammographic test objects over a wider range of exposures than did standard mammographic film screen systems. This information was included in our Annual Report to the U.S. Army in 1994. This was determined by our systematic response surface optimization experiments and was reported in 1995. (Freedman, 1995 B).



This chart demonstrates that at mAs less than 25, while the storage phosphor system could demonstrate objects, the screen film failed to demonstrate any of the objects. At 25 and 32 mAs, the storage phosphor demonstrated smaller objects than screen film. At 32, 40, and 80 mAs, the two systems performed equivalently. (Storage = Storage Phosphor Radiography. GA = gradient angle of the look up table.) These results indicate that there is information available that can be captured by the storage phosphor plate that correlates to those regions seen in mammograms as radiodense (clear or almost clear) regions of the image. (From Freedman, 1995 B)

Although we knew of this phenomenon in 1993, we did not have a clinically useful method of retrieving this information for display in a clinical setting. If we attempted to include the full range of information in a single image, the resulting image was of low contrast and not clinically useful. If we attempted to post-process the images so that one image reflected the high exposure image and another the low exposure image, the Fuji PRIEF prevented it. In June 1994, I requested Fuji to modify their software so that I could test a system for bypassing the PRIEF effect using the Dynamic Range Control (DRC) system software with special DRC curves. These curves were provided in the Spring of 1995 but resulted in system crashes. The modified software became available in the Summer of 1995. The effect of DRC using these new curves was to provide images that contain both levels of exposure data in a single image. Examples of the new processing are attached to this report (Appendix 5).

Although the math is more complex, the easiest way to understand the effect of DRC in mammography is to consider it a complex form of image processing. In this image processing, the image is separated into two images: a low frequency mask and an original image. Histogram equalization is then performed on the low frequency mask and this mask is then subtracted from the original image. This final image shows a decreased range grayscale of pixel values that covers large regions of the image, but leaves intact the pixel values of high spatial frequency regions. Since the high frequency regions represent the microcalcifications and edges of most masses, the resulting image provides the ability to see the high frequency structures of the breast potentially from the skin line to the most dense regions of the breast (as shown in figure 1) while preserving the visibility of microcalcifications.

There are three types of modification of the look-up table that are possible. These are explained in a pre-print of a paper to be presented at SPIE Medical Imaging 1996 (which is attached as Appendix 6).

The Fuji software still imposes limits so that we cannot produce the optimal image automatically and some cases show the effect better than others. Currently, we cannot reprocess images retrieved from the optical disk drive, but only those still stored as original data on the Fuji 254 workstation hard disk, but have requested a software modification from Fuji Japan to allow this. We were recently notified that the Fuji Development Center in Japan will be supplying this software upgrade in April 1996. We have, however, been able to partially mimic this effect using wavelet transforms and are working to improve this. We are also working with Fuji to better define the applications of this algorithm. We believe that this will allow us to better image the radiodense breast allowing us to see microcalcifications and possibly masses better than on-screen film mammography. If we are correct in our analysis, this new form of digital mammography may improve the sensitivity of mammography for the detection of breast cancer in women under the age of 50. Since 37% of the breast cancer new cases seen at Georgetown occur in this age group and the current sensitivity of mammography in this age group is 60-68% (compared to 90% in women over the age of 50), we consider this a most important development.

Digital Mammography and The Shape of Microcalcifications

Concern has been expressed that digital mammography at 100 micron pixel size will not allow sufficient information about the shape of microcalcifications to be seen. Based on this concern, we have recently performed an experiment in which we compared the original screen film mammogram, the 100 micron pixel storage phosphor mammogram and the biopsy specimen radiograph in 10 randomly selected cancer cases and 10 randomly selected benign biopsy proved cases. All cases contained microcalcifications. Four radiologists indicated their preferences between the screen film and digital images. A preprint of this report is attached as Appendix 7. Briefly, the four radiologists expressed preference in the majority of cases for the digital system in microcalcification conspicuity. One of the four preferred the digital images for shape and number of microcalcifications, one considered each system preferable in an equal number of cases, and two preferred the screen film system. Whatever the radiologists preferences, the radiologists were unable to distinguish benign and malignant cases on either the digital or conventional systems. Thus, although there may be a slight preference for evaluation of shape on the conventional system, this preference did not appear to be of clinical importance since it did not help the radiologists to better classify the benign or malignant features associated with the calcifications.

The improved conspicuity of microcalcifications found by the radiologists with the digital systems suggests that these systems may prove to be better than screen film mammography in a screening setting. We are working to obtain funds for such a full scale screening test.

Current Recommendations for the Implementation of Digitized Film Mammography

We have been unable to define an adequate system for acquisition, image processing, and display for digitized film mammography that is diagnostically equivalent to conventional screen film mammography. In the current year, we will be testing better hard copy display systems for digitized film mammography.

Current Recommendations for the Implementation of Direct Digital Mammography

Image Acquisition

Image acquisition with either the Fuji 9000 or Fuji AC-3 appears adequate for diagnostic mammography. An ROC study to be performed in the first half of 1996 is expected to confirm this. The Fuji AC-1 provides a lower quality image than the Fuji 9000 and the AC-

3. The lower signal to noise ratio of the AC-1 results in noisier images. It is possible that using higher exposures with the AC-1 could provide adequate images, but we have not tested that hypothesis since we would then have to exceed the standard dose used for conventional screen film mammography. The Fuji system is not FDA approved for mammography. In October 1995, the FDA published draft guidelines for those seeking approval of digital mammography systems. We submitted comments on their proposal. The final guidelines are not yet released. The guidelines resulted from a meeting the FDA held March 6, 1995. The PI of this project was one of the experts testifying at the FDA hearing. (Appendix 8)

A more extensive trial will be necessary to meet FDA recommendations for screening mammography. Although the FDA has not yet published its final recommendations, it seems likely that a sample of 10,000 clinical cases will be necessary.

The Fuji systems use a 100 micron pixel size which appears adequate. Tests of a commercially available 50 micron pixel small field system showed that the 50 micron system required a higher radiation exposure and while it provided higher contrast, it did not allow the detection of smaller objects. We believe that the 50 micron system we tested can be improved upon and that the eventual 50 micron system may prove to be superior to the 100 micron system we currently use.

Image Processing

Fuji image processing modified to the following parameters appears to provide adequate display for hard copy direct digital mammography. An ROC study will be performed shortly to confirm this statistically. Application of special DRC methods appears potentially to provide improved imaging of the radiodense breast. Additional investigation of this new image processing method is underway.

GA=1.2, GT=G, GS=0.6, GC=0.3 RN=7, RT=R, RE=0.0

Image Display

Hard Copy Display: Display with the Fuji FL-IM 3543 printer appears adequate, but not optimal. Display on the Polaroid Helios printer and 3M 969 printers result in better image appearance, but it is not yet shown that they affect diagnostic accuracy. The newest Fuji printer FL-IM D has not yet been tested by us, but in images of digital mammograms we have seen from other sites appears very promising.

Soft Copy Display: Tests are currently underway.

Current Status of Items in Statement of Work

1. Recommended resolution size for digitized film mammography

Using existing technology, we have been unable to define a system configuration that will provide diagnostic information equivalent to conventional screen film mammography. We have more extensively tested 100 micron digitization and have shown it to be inferior to screen film in the display of microcalcifications. We have been unable to come up with a reasonable clinical scenario for the display of 50 micron digitized film.

We expect to test further, in 1996, the laser print display of 50 and 100 micron digitized film mammography using new state of the art laser film printers and will report on this in our final report.

2. Coordinating the testing of these parameters with the associate military sites

The image quality of the digitized film mammographic images has been sufficiently unsatisfactory that the military sites were not asked to participate--we did not wish to waste their time. We have involved them in a different project involving computer aided diagnosis which is reported in the appropriate army grant # DAMD17-93-J-3007 annual report.

We will be incorporating Army physicians in the design and implementation of the ROC study of direct digital mammography that is about to begin.

3. Implementation document for direct digital mammography

We have defined the image acquisition parameters, image processing parameters and factors for display of direct digital mammography. These will be incorporated into the final report. Colonel Ted Raia, MD at WRAMC has agreed to have WRAMC serve as a test site for direct digital mammography to be managed by Major Morgan Williamson, MD. We will be setting up with them a prospective clinical trial of direct digital mammography to be performed at WRAMC and Fort Belvoir,Virginia. The purpose of this trial will be to compile the data for FDA approval. We are currently awaiting the FDA response to comments on their draft recommendations on the performance of digital mammography clinical trials and for the FDA's final recommendations.

Conclusion

Work to optimize the appearance of digitized film mammography and digital mammography using storage phosphor technology is nearly complete. The attached report and its appendices indicate that digitized film mammography (digitized at 100 micron pixel size) is insufficient for clinical interpretation with soft copy display. Hard copy display is still insufficient, however, we are planning tests of a newer method for hard copy display during the coming (final) year of the project. Digital mammography using storage phosphor methods has been optimized and an ROC analysis of this method using our current data set of approximately 30 proven cancer cases and a matched number of benign cases is about to begin. This ROC study will compare matched conventional and digital images using six radiologists. Each of the cancer and benign finding cases is pathologically proven. We are also exploring special image processing methods for the radiodense breast and these are discussed in this report. An analysis of the shape of microcalcifications comparing conventional and digital mammography using a 100 micron pixel size has been completed and shows that there is general preference for the conspicuity of microcalcifications on digital mammography. Analyses of shape and number of microcalcifications resulted in varying opinions from the four radiologists doing the comparisons. Whichever system the radiologists preferred, they were unable to differentiate benign from malignant in this series so any slight differences in shape visibility did not seem to affect classification.

References/Bibliography

1. Dawkins T, Freedman M, Lo S-C B, Mun S K: 35 Micron CCD Based Film Digiter for Mammography. SPIE Poster. SPIE Medical Imaging paper 1897-53 (February 1993).

2. Freedman M, Mun S K, Pe E, Weiser J C, Roblein J R, Lo S-C B, Nelson M: Quality Control of Storage Phosphor Imaging Devices. CAR 93, 7th International Symposium Berlin (June 24-26, 1993); 456-460pp.

3. Freedman M, Pe E, Nelson M, Lo S-C B, Mun S K: Digital Mammography: Demonstration of a Method of Achieving Adequate Resolution on a Storage Phosphor System. CAR 93, 7th International Symposium Berlin (June 24-26, 1993); 783pp.

4. Wu Y C, Lo S-C B, Zuurbier R, Hasegawa A, Freedman M, Mun S K: Classification of Microcalcifications Using A Hybrid Neural Network. SPIE: Medical Imaging (February 1994). Paper 2167-61.

5. Fields F, Freedman M, Lo S-C B, Zuurbier R, Nelson M, Mun S K: Comparison of Conventional Film Screen Magnification Mammography and Electronic Magnification. SPIE: Medical Imaging (February 1994). Paper 2167-67.

6. Romlein J, Leckie R, Smith S, Quillin E, Freedman F: Evaluation of Specific PACS Equipment Components Operational and Maintenance Experience. SPIE: Medical Imaging, Vol. 2164 (1994), 198-208pp.

7. Lo S-C B, Kim M-B, Li H, Krasner B, Freedman M, Mun S K: Radiological Image Compression: Image Characteristics and Clinical Considerations. SPIE: Medical Imaging, Vol. 2164 (1994); 276-281pp.

8. Freedman M, Pe E, Zuurbier R, Katial R, Jafroudi H, Nelson M, Lo S-C B, Mun S K: Image Processing in Digital Mammography. SPIE: Medical Imaging, Vol. 2164 (1994); 537-554pp.

9. Freedman M, Steller D, Jafroudi H, Lo S-C B, Zuurbier R, Katial R, Hayes W, Wu Y C, Lin J-S J, Mun S K: Digital Mammography: Effects of Decreased Exposure. SPIE: Medical Imaging (1995). Paper 2432-49.

10. Freedman M, Steller D, Jafroudi H, Lo S-C B, Zuurbier R, Katial R, Hayes W, Wu Y C, Lin J-S J, Steinman R, Tohme W G, Mun S K: Digital Mammography: Tradeoffs Between 50- and 100-micron Pixel Size. SPIE: Medical Imaging (1995). Paper 2432-09

11. Hasegawa A, Lo S-C B, Wu Y C, Lin J-S J, Freedman M, Mun S K: Adaptive size Neural-networks based Computer-aided Diagnosis of Microcalcifications. SPIE: Medical Imaging (1995). Paper 2434-63.

12. Jafroudi H, Steller D, Freedman M, Mun S K: Quality Control on Storage Phosphor Digital Radiography System. SPIE: Medical Imaging (1995). Paper 2432-59

13. Steller D, Jafroudi H, Freedman M, Mun S K: Performance and Maintenance of Storage Phosphor Plates and Cassettes in Digital Radiography. SPIE: Medical Imaging (1995). Paper 2432-60.

14. Freedman MT, Steller D, Jafroudi H, Mun SK. Quality Control of Storage Phosphor Digital Radiography Systems. J Digital Imaging 1995. 8:67-74

15. Lo SCB, Chan HP, Lin JS Li H, Freedman MT, Mun SK. Artificial Convolutional Neural Network for Medical Image Pattern Recognition. Neural Networks, 1995, Accepted for Publication.

16. Wu YC, Freedman MT, Hasegawa A, Zuurbier RA, Lo SCB, Mun SK. Classification of microcalcifications in radiographs of pathologic specimens for the diagnosis of breast cancer. Academic Radiology 1995;2:199-204.

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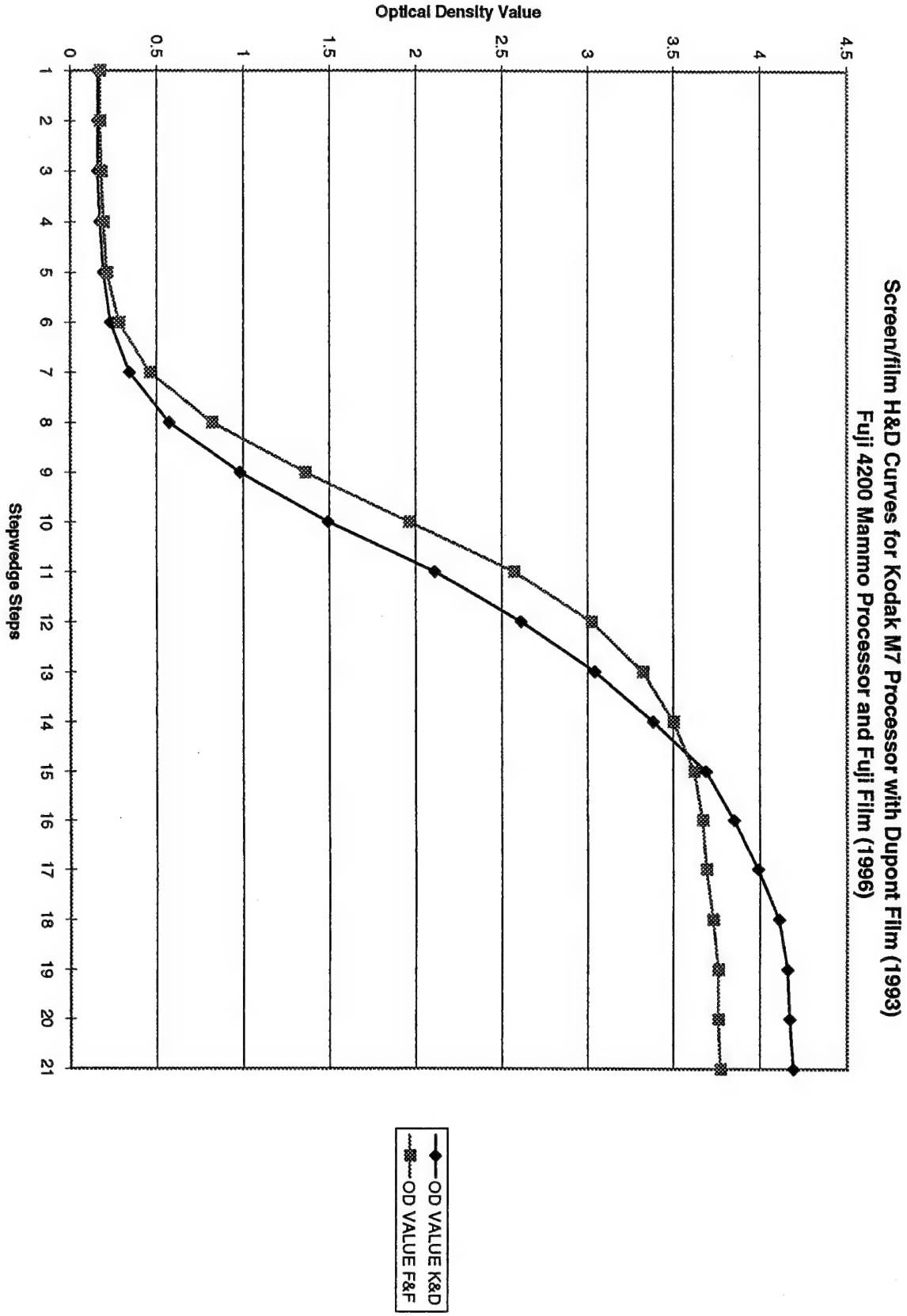
7. Digital Mammography: An evaluation of the Shape of Microcalcifications

8. Digital Mammography: Presentation for the Food and Drug Administration Panel on DigitalMammography, March 6, 1995


Screen/film H&D Curves for Kodak M7 Processor with Dupont Film (1993)
Fuji 4200 Mammo Processor and Fuji Film (1996)
Optical Density Value
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Stepwedge Steps
OD VALUE K&D
OD VALUE F&F

Implementation and Testing of Digital Mammography for MDIS Environment

December 31, 1995

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1. INTRODUCTION

1.1. Objective

The objective of this project was to evaluate image quality of digital mammography based on computed radiography (CR) and high resolution film digitizer and develop a strategy to implement digital mammography into the military diagnostic imaging systems (MDIS) environment.

1.2. Project Schedule

Start Date: October 1, 1994
End Date: December 31, 1995
There are total 15 months which are divided into 5 quarters.

First Quarter (October 1, 1994 - December 31, 1994)
Budget request: 40%
Goals:
1. Set up of an experimental system.
2. Study of physics characterization of data acquisition modules.
3. Data collection and database management.

Second Quarter (January 1, 1995 - March 31, 1995)
Budget request: 20%
Goals:
1. Collection of 10 clinically relevant cases in all modalities.
2. Comparative reading of 10 cases in hard copy and soft copy.

Third Quarter (April 1, 1995 - June 30, 1995)
Budget request: 20%
Goals:
1. Collection of 10 clinically relevant cases in all modalities.
2. Comparative reading of 10 cases in hard copy and soft copy.
3. Technical evaluation of MDIS database to determine suitability for digital mammography.

Fourth Quarter (July 1, 1995 - September 31, 1995)
Budget request: 10%
Goals:
1. Collection of 20 clinically relevant cases in all modalities.
2. Comparative reading of 20 cases in hard copy and soft copy.
3. Determination of MDIS workstation functionality for digital mammography.

Fifth Quarter (October 1, 1995 - December 31, 1995)
Budget request: 10%
Goals:
1. Comparative reading of 10 cases in hard copy and soft copy.
2. Data analysis.
3. Final report.

1.3. Participants

- Case selection
  - Rebecca Zuurbier, M.D., Director of Breast Imaging, GUMC
  - Jaquelyn Hogge, M.D., Mammographer, GUMC
- Collection of Fuji CR9000 and screen film mammograms - Dot Artz, R.T., R.M.
- Digitization of screen film mammograms - Two part time students of Georgetown University
- Data management and image processing - Jyh-Shyan Lin, Ph.D., ISIS Center, GUMC
- Vicom display workstation - Akira Hasegawa, Ph.D., ISIS Center, GUMC.
- Comparative reading - Five board-certified radiologists of Radiology Department, GUMC
  1. Matthew T. Freedman, M.D., M.B.A. - Clinical Director of ISIS Center
  2. Rebecca Zuurbier, M.D. - Director of Breast Imaging
  3. Jaquelyn Hogge, M.D. - Mammographer
  4. Wendelin Hayes, D.O. - Associate Professor of Radiology
  5. Curtis Green, M.D. - Radiologist

2. EXPERIMENTAL SYSTEM CONFIGURATION

2.1. Set up of an Experimental System

The experimental system configuration is shown in Figure 1. The key components are: a Fuji CR9000 (FCR9000), a Lumisys film digitizer, a data acquisition and system management (DASM) host Sun workstation, a digitizer host Sun workstation, and a Vicom high resolution display workstation.

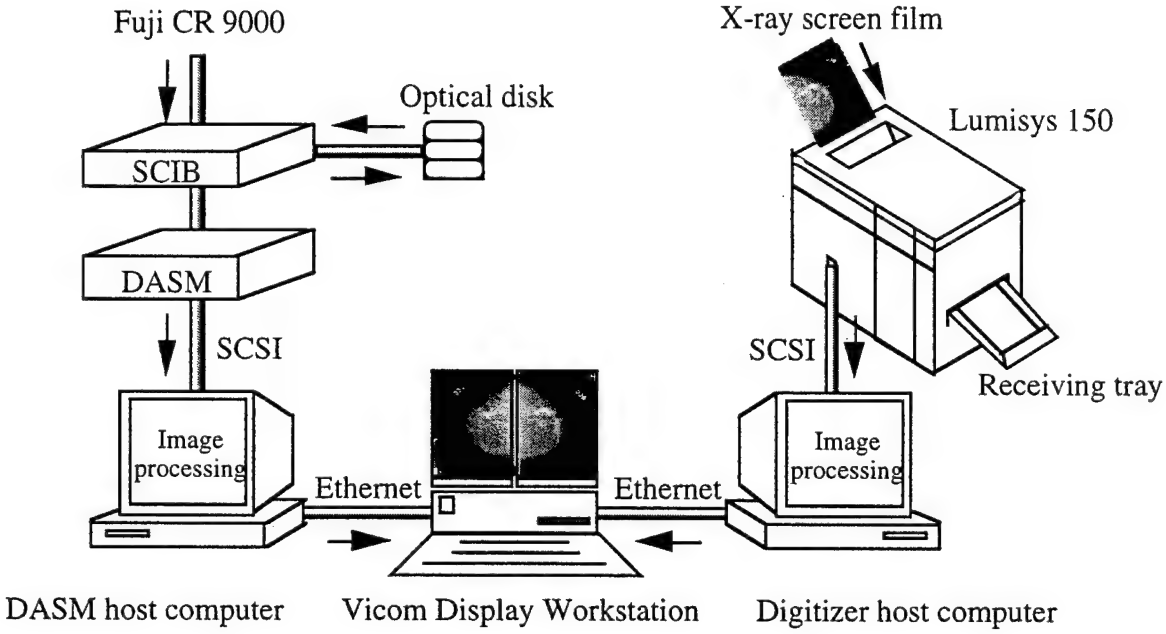
The Fuji Computed Radiography 9000 System

The DASM controls the data transfer from the FCR9000 to the host Sun workstation through the small computer system interface (SCSI) cable. Each CR image contains a 2048 bytes image header. The CR images were then processed and transferred to the Vicom display workstation. A second channel interface board (SCIB) was installed for the purpose of simultaneously interfacing with DASM and an optical disk device. Original CR images including biopsy specimen were backed up in the optical disks.

The Lumisys 150 High Resolution Laser Film Digitizer

Conventional screen films (SF) were digitized by a Lumisys high resolution film digitizer. Digitized SF images were transferred to the digitizer host Sun computer through the SCSI, processed, and then transferred to the Vicom display workstation.

- The Lumisys 150 meets the film digitizer requirements by MDIS which are variable spot size, different film sizes (from 8" × 10" up to 14" × 17"), minimum spot size of 210 microns, and 10 bits minimum dynamic range (i.e., 10 bits per pixel). The density resolution and precision is a linear function from 0 to 3.5 optical density (OD). The Lumisys 150 film digitizer can determine the film size automatically. It can convert films sized from 8" × 10" up to 14" × 17" into digital images of 2048 pixels × 2560 lines with 12 bits per pixel (10 Mbytes). The 8" × 10" films can also be digitized at 50 μm spot size which is equivalent to 4096 pixels × 5120 lines with 12 bits per pixel (= 40 Mbytes). The laser spot size can be auto-adjusted accordingly.
- The Lumisys 150 does not provide automatic sheet feeder. A more advanced Lumisys 200 digitizer will have the function of automatic sheet feeder which is able to hold and automatically feed at least 10 x-ray films of intermixed sizes. The digitizer generates two file formats: raw binary image and TIFF compressed images for image preview. The image previewing software is the x-window view (XV) software program run on the SUN digitizer host computer. The Lumisys 150 does not support the American College of Radiology (ACR)-National Electrical Manufacturers Association (NEMA) standard.
- Phantoms, such as CIRS, ACR, CDMAM, step wedge, and SMPTE, were digitized at 50 micron and 100 micron and displayed on the Vicom display workstation. The Lumisys digitized phantoms showed satisfactory quality.
- The Lumisys high resolution digitizer (Model: 150) is set up to digitize conventional SF at 100 μm resolution. Currently, the Lumisys digitizer is now located in the mammography reading room in Georgetown University Medical Center (GUMC) and is being used routinely to digitize clinical cases. Each clinical case consists of four recent and four previous mammograms with pathology reports.
- The Vicom display workstation is a Pixar-based system which has four high resolution MegaScan monitors. Each display monitor can display image data of 2048 × 2560 × 8 bits. The display workstation provided window-and-level function for adjustment of image brightness and contrast. Each monitor can be manipulated individually.



DASM: data acquisition and system management
SCSI: small computer system interface
SCIB: second channel interface board

Figure 1. Experimental System Configuration.

2.2. Study of Physics Characteristics of Data Acquisition Modules

• Quality control (QC) on a Fuji printer and a Fuji CR9000

• QC of 18 cm × 24 cm image plate (IP):

Every morning each 18 cm × 24 cm IP received secondary erasure through FCR 9000 to ensure that a properly erased IP was in each cassette before any images were obtained. This process reduces possible residual radiation in the plate and ensures the best possible image.

• QC of Fuji 9000 laser printer (LP):

Every morning a cleaning film was run through the LP, then the density and check density were adjusted. A step wedge was produced from both steps. After the step wedge pattern is obtained from the check density, the optical density values was displayed on the LP display. The values and graph similar to sensitometry graph for a film processor were recorded.

• QC of mammography film processor:

Normal sensitometry graphing, cassette cleaning, exposure monitoring were performed according to ACR standard.

The quality control for mammography film processor and Fuji LP was performed by in-house engineering.

• Lumisys Film Digitizer and the Vicom Display Monitors

• Lumisys film digitizer:

We have performed maintenance of the Lumisys scanner periodically. The maintenance includes dust removal of the reflection mirror, the pinch roller, and the aperture of the detector, and adjustment of the voltage of both the main and the reference detectors [1]. The digitizer is also calibrated based on a Lumisys test pattern. The maintenance is to assure the digitization quality and calibration of the digitizer.

• Vicom workstation:

The Vicom system has four 2k × 2.5k display monitors. Each monitor can display a full data set of a 8 × 10" mammogram digitized at 100 micron. The brightness is 60 foot-Lamberts and the gray level is 256 shades. Since there is no single set of window (i.e., contrast) and level (i.e., brightness) values for every image display, the look-up table of the system was preset to a set of window and level values visually determined by a physicist, a registered mammographer, and a scientist. The purpose is to adjust the two monitors such that they have similar intensity and contrast. The contrast and brightness can be adjusted by using a trackball during the study of comparative reading.

3. DATA COLLECTION AND MANAGEMENT

3.1. Case Selection and Data Collection Protocol

The database used in this study included 50 cancerous and non-cancerous cases. All the cases contained bilateral breast images, radiology reports, and related pathology reports. Biopsy was used as the standard proof of cancer or non-cancer. Each set of bilateral mammograms contained either left-right cranio caudal (CC) or left-right mediolateral oblique (MLO) views. We collected 50 CR soft copies, 50 CR hard copies, 50 SF hard copies, and 50 soft copies of digitized films. Table 1 lists the collected database of the 50 clinically relevant cases. The table shows fake patient identification numbers (ID) for patient confidentiality. A similar table with real patient name and ID is available and kept securely at GUMC. In the table, "BRST" represents breast, "BX" represents biopsy, "MAMMO" means mammogram, and "POS FOR CA" means positive for cancer. One half of the cases contained microcalcifications, one half of cases contained masses, and some cases of architecture distortions were included. Films were digitized in such a way that most patient demographic data were excluded.

3.2. Data Management

- The Lumisys model 150 film digitizer was set up at 100 micron scanning mode.
- Actual size of hard copy:
  - Hard copy SF: 8 inch × 10 inch.
  - Hard copy CR: 11 inch × 14 inch.
- Actual size of soft copy:
  - 100 micron/pixel for the CR soft copies.
  An image size is 8,404,136 bytes (including image header) per CR soft copy.
  - 100 micron/pixel for the soft copies of digitized SF.
  An image size is 10,485,760 bytes (including image header) per digitized SF.
- The soft copies of SF and CR both contain 2,048 bytes image header.
- Storage of soft copies: DEC optical disks (595 MB per optical disk).
  A set of two digitized films (left and right breasts) and two soft copies of CR (left and right breasts) has approximately 40 Mbytes, hence for 50 cases of processed and non-processed images we ned 50 cases × 40 Mbytes/set × 2 = 4 Gbytes = 8 DEC optical disks. For other ISIS research projects, such as the classification of benign and malignant microcalcifications, we have also digitized the mammograms at 50 μm resolution using the Lumisys film digitizer. Digitized image data were stored on optical disks as well as a Hewelett-Packard (HP) jukebox.

3.3. Image Processing Protocol

- Decode the image headers of Lumisys digitized images.
- Encode image data - rearrange display scanning lines.
- Attach Pixar II image header.
- Move images to the fast disks of Vicom workstation for display.

Table 1 Database of 50 Clinical Relevant Cases

ID #	DATE	DIGITAL VIEWS	BRST FOR BX	MAMMO FINDINGS	PATHOLOGY RESULTS	POS FOR CA
1	6/8/95	Bilat. CC	Left	Ca++	1mm ductal CA +DCIS	yes
2	9/29/95	Bilat. CC	Right	mass	fibroadenoma	no
3	12/12/94	Bilat. CC	Left	mass	fibrocystic changes	no
4	12/8/94	Bilat. CC	Right	spic. mass with Ca++	intraductal CA	yes
5	1/24/95	Bilat. CC	Right	Ca++	invasive intraductal CA	yes
6	7/13/95	Bilat. CC	Right A73	small mass	ductal hyper. Ca++	no
7	12/20/94	Bilat. CC	Right	spic. mass	ductal hyper. Ca++	no
8	3/3/95	Bilat. MLO	Right	mass	ductal hyperplasia	no
9	6/12/95	Bilat. CC	Left	mass with Ca++	fibrocystic changes	no
10	6/1/95	Bilat. CC	Left A111	mass with Ca++	small fibroadenoma	no
11	8/24/95	Bilat. CC	Bilat.	Ca++	intraductal CA	yes
12	7/24/95	Bilat. CC	Right A90	Ca++	intraductal CA	yes
13	6/19/95	Bilat. CC	Right A48	multiple masses	fibrocystic changes	no
14	6/2/95	Bilat. CC	Left	mass	8mm infiltrating ductal CA	yes
15	6/23/95	Bilat. CC	Right	micro Ca++	stromal fibrosis	no
16	6/12/95	Bilat. CC	Left	mass	small fibroadenoma	no
17	6/23/95	Bilat. CC	Left A58	Spic. mass with Ca++	1.radial scar 2. ID CA	yes
18	7/31/95	Bilat. CC	Right A113	Ca++	radial scar with ID CA	yes
19	7/11/95	Bilat. CC	Right A98	scattered Ca++	cystic change Ca++	no
20	3/10/95	Bilat. CC	Right A55	Ca++	normal	no
21	8/2/95	Bilat. CC	Right A113	posterior Ca++	intraductal CA	yes
22	4/24/95	Bilat. CC	Right A64	dense mass	3cm papil. ductal CA	yes
23	12/12/94	Bilat. CC	Right	Ca++ at prev. surg. site	intraductal CA	yes
24	2/3/95	Bilat. CC	Left	Ca++	fibrosis	no
25	3/6/95	Bilat. MLO	Left	Ca++	intraductal CA insitu atyphyper.	yes
26	12/29/94	Bilat. CC	Left	mass with ?Ca++	fibroadenoma	no
27	6/29/95	Bilat. CC	Right	mass/prev. CA	atypical intrduct. hyperp.	no/yes
28	7/20/95	Bilat. CC	Right A152	mass	invas.ductal CA with Ca++	yes
29	12/8/94	Bilat. CC	Right	spic. mass with Ca++	intraductal CA	yes
30	6/22/95	Bilat. CC	Right A70	Ca++	intraductal papill.	no
31	2/27/95	Bilat. CC	Right	subtle Ca++	ductal hyper. Ca++	no
32	12/8/94	Bilat. CC	Right	mass	ductal hyperplasia	no
33	10/9/95	Bilat. CC	Right+Left	masses	infiltrating ductal CA	yes
34	8/17/95	Bilat. CC	Left	SUBTLE microCa++	extensive ductal CA insitu	yes
35	12/16/94	Bilat. CC	Right	Ca++ dense tissue	intraductal CA	yes
36	6/6/95	Bilat. CC	Left	mass	infiltrating ductal CA	yes
37	6/12/95	Bilat. CC	Right	mass	fibroandenoma	no
38	12/5/94	Bilat. CC	Left	spic. mass with ?Ca++	intraductal CA	yes
39	12/27/94	Bilat. CC	Left	casting Ca++	fibrocystic changes	no
40	6/22/95	Bilat. CC	Right A108	2 masses	5mmand9mm invas.duct CA	yes
41	6/1/95	Bilat. MLO	Left A74	mass with Ca++	fibrocystic change	no
42	7/28/95	Bilat. CC	Left A116	Ca++	fibrocystic change Ca oxalate	no
42	3/6/95	Bilat. CC	Left	Ca++	hyperplasia	no
44	7/11/95	Bilat. MLO	Right A88	palpable mass not seen	no lesions indentified	no
45	7/13/95	Bilat. CC	Bilateral R A154	Ca++	R-early insitu L-fibrocyst.	yes-no
46	11/22/94	Bilat. CC	Right	spic. mass with Ca++	infiltrating CA	yes
47	1/13/95	Bilat. CC	Left	Ca++	ductal CA in situ	yes
48	8/17/95	Bilat. MLO	Left	hx nodular fascitis (benign)	mass excised no bx report	no
49	12/15/94	Bilat. CC	Left	nodule	fibrocystic changes	no
50	11/17/95	Bilat. CC	Right	subtle Ca++mid post.	intraductal CA comedo type	yes

4. COMPARATIVE READING

4.1. Preference Study of Hard Copy and Soft Copy of Screen Films

We performed a preference study to evaluate image quality of digital mammography derived from conventional screen films (i.e., hard copies) and a high resolution film digitizer (i.e., soft copies). We wanted to compare one view (either CC or MLO) of original mammograms with the digitized film at 100 micron spatial resolution. The SF hard copies were digitized and directly converted to Vicom format (see Section 3.3 Image Processing Protocol). Five board-certified radiologists, Dr. Wendelin Hayes (radiologist 1), Dr. Jaquelyn Hogge (radiologist 2), Dr. Matthew T. Freedman (radiologist 3), Dr. Curtis Green (radiologist 4), and Dr. Rebecca Zuurbier (radiologist 5), participated in this study of preference reading of soft and hard copies.

• **Set up of environment for human readers**

The reading environment for human readers was set up as follows:

- Low level ambient light.
- No time limit in the comparative reading of each case.
  - Radiologists can use trackball to control the window-and-level while viewing soft copies on the Vicom monitors. Note that, in this study, the window-and-level was controlled by the principal investigator while the radiologist requested the change of the intensity and contrast of the displayed images.
- Light box was used with emulsion side facing the reader.
- Human readers have to fill out the questionnaires (see Section 4.2) provided in this study
- Pairs of hard and soft copies of an SF will be displayed on the light box and two Vicom monitors, respectively (Figure 2). The human readers filled out the questionnaire.
- Hard copies and soft copies are both displayed in anatomically corrected views.
- Each hard copy was labeled as #1, #2, etc. The patients' demographic data on the screen films were covered up (on the dull side of the SF) by using black electrical tape.

• **Comparative reading and reading-order effects**

- Sample size (Table 1): 25 cases of proven biopsy cancer and 25 cases that appeared malignant but were proven by biopsy to be benign.
- In the first 25 cases, two of the human observers first read hard copies and then soft copies of the SF while the other three read the two modalities in the opposite order. In the second 25 cases, the two of the human observers read soft copies of the SF first and then hard copies while the other three read the two modalities in the opposite order. The purpose of this reading order arrangement was to reduce the *reading-order effects* [2]. The reading-order effects result in the biases that occur in a situation when two or more equivalent images of a particular patient are read in different order by the same observer. It is normally the case that the image read last will tend to be interpreted more accurately than the image read first if any relevant information is retained by the observer from a reading of one image of the patient to the next.
- During the comparative reading, the radiologist can always look back-and-forth to the two image modalities retrospectively and repeatedly.
- The questionnaire contained nine questions with check mark areas. If no lesions, such as microcalcifications (questions 1 and 2), masses (question 3 and 4), and asymmetric densities (questions 5 and 6), were found, the check mark areas were left blank. On the other hand, if both hard and soft copies of SF were equally well rated, both areas were marked.

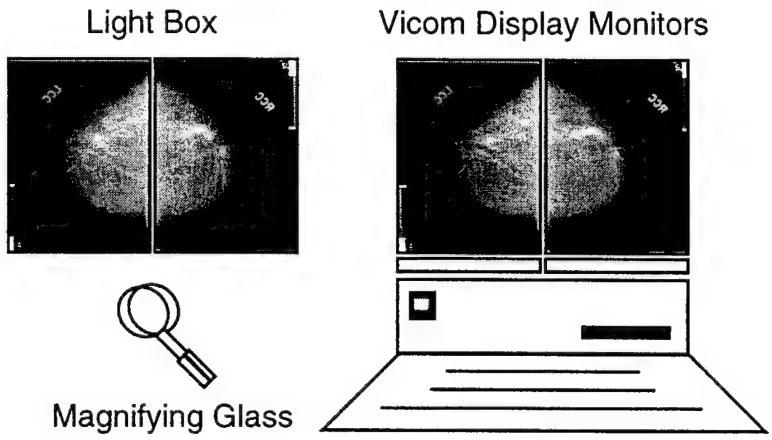


Fig. 2. Comparative Reading.

4.2. Questionnaire for Comparative Reading

Soft copy *vs.* Hard copy of SF

Viewer initial: _____ Date: _____

1. On which do you detect microcalcifications better?
   Hard copy _____ or soft copy _____.

2. Which one better characterized the microcalcifications as to malignant *vs.* benign?
   Hard copy _____ or soft copy _____.

3. On which do you detect masses better?
   Hard copy _____ or soft copy _____.

4. Which one better characterized the masses as to malignant *vs.* benign?
   Hard copy _____ or soft copy _____.

5. On which do you detect asymmetric density better?
   Hard copy _____ or soft copy _____.

6. Which one better characterized the asymmetric density?
   Hard copy _____ or soft copy _____.

7. Do you have a preference? Hard copy _____ or soft copy _____.

8. Do you see anything of clinical importance on the hard copy that you do not see on the soft copy? Yes _____ or No _____

If yes, what? _____

9. Do you see anything of clinical importance on the soft copy that you do not see on the hard copy? Yes _____ or No _____

If yes, what? _____

*Comment: _____

5. QUESTIONNAIRE RESPONSES AND DATA ANALYSIS

5.1. Questionnaire Responses

From the questionnaire (a pair of soft vs. hard copies of SF), we obtained histogram bars of the number of soft and hard copies of SF which better characterize microcalcifications, masses, and asymmetric density as to malignant *vs.* benign. Moreover, we will have the number of preferred soft and hard copies of the five human readers. The five radiologists' responses to the specific questions in the questionnaire are shown in Table 2.1 - Table 2.5 and Figure 3.1 - Figure 3.5. In each table, the columns of Q1 - Q9 represent answers for questions 1 through 9 for the 50 cases, H represents hard copy, S represents soft copy, Y means yes, and N means no. The answer "both" or "H/S" means that there was no preference, i.e., both hard and soft copies were equally well accepted. The blank and the answer "neither" mean that the question was not applicable, i.e., the disease patterns were not seen. In each Figure 3.1 - 3.5, R1 - R9 represent responses to Q1 - Q9, respectively, H means hard copy and S means soft copy.

For all the questions 1 - 7, Dr. Freedman prefers hard copy to soft copy in all cases.
For all the questions 1 - 6, Dr. Zuurbier prefers hard copy to soft copy in all cases.

Responses to question 1:
- On which do you detect microcalcifications better?
Dr. Green prefers hard copy to soft copy in 38 calcification cases and no preference in 12 cases.
Dr. Hayes prefers hard copy to soft copy in all calcification cases.
Dr. Hogge prefers hard copy to soft copy in 47 calcification cases and no preference in 3 cases.

Responses to question 2:
Which one better characterized the microcalcifications as to malignant *vs.* benign?:
Dr. Green prefers hard copy to soft copy in all 37 calcification cases and no preference in 13 cases.
Dr. Hayes prefers hard copy to soft copy in calcification cases.
Dr. Hogge prefers hard copy to soft copy in 48 calcification cases and no preference in two cases.

Responses to question 3:
- On which do you detect masses better?
Dr. Green prefers hard copy to soft copy in 6 mass cases and no preference in 26 cases.
Dr. Hayes prefers hard copy to soft copy in 23 mass cases and soft copy to hard copy in 6 cases.
Dr. Hogge prefers hard copy to soft copy in 5 mass cases, soft copy to hard copy in 10 cases, and no preference in 35 cases.

Responses to question 4:
- Which one better characterized the masses as to malignant *vs.* benign?
Dr. Green prefers hard copy to soft copy in 11 mass cases and no preference in 21 cases.
Dr. Hayes prefers hard copy to soft copy in 28 mass cases and soft copy to hard copy in one case.
Dr. Hogge prefers hard copy to soft copy in 4 mass cases, soft copy to hard copy in 8 cases, and no preference in 38 cases.

Responses to question 5:
- On which do you detect asymmetric density better?
Dr. Green prefers hard copy to soft copy in 3 asymmetric density cases and no preference in 18 cases.

Dr. Hayes prefers hard copy to soft copy in 6 asymmetric density cases and soft copy to hard copy in 2 cases.
Dr. Hogge prefers hard copy to soft copy in 5 asymmetric density cases, soft copy to hard copy in 14 cases, and no preference in 31 cases.

Responses to question 6:
- Which one better characterized the asymmetric density?
Dr. Green prefers hard copy to soft copy in 8 asymmetric density cases and no preference in 14 cases.
Dr. Hayes prefers hard copy to soft copy in all asymmetric density cases.
Dr. Hogge prefers hard copy to soft copy in 4 asymmetric density cases, soft copy to hard copy in 9 cases, and no preference in 37 cases.

Responses to question 7:
- Do you have a preference?
Dr. Green prefers hard copy to soft copy in all 50 cases.
Dr. Hayes prefers hard copy to soft copy in 48 cases, soft copy to hard copy in one case, and no preference (i.e., equally well accepted) in one case.
Dr. Zuurbier prefers hard copy to soft copy in 45 cases and no preference in 5 cases.
Dr. Hogge prefers hard copy to soft copy in 36 cases, soft copy to hard copy in 8 cases, and no preference in 6 cases.

Responses to question 8:
- Do you see anything of clinical importance on the hard copy that you do not see on the soft copy?
The five radiologists saw microcalcifications on the hard copy that they did not see on the hard copy. Sometimes dramatic window-and-level adjustment may enhance the subtle microcalcifications, however, the other breast will become either too dark or too bright. Though both masses and architecture distortion can be seen on the soft copies, they seem to increase the perception of normal soft tissue structures as abnormal .

Responses to question 9:
Do you see anything of clinical importance on the soft copy that you do not see on the hard copy?
The five radiologists saw microcalcification-like objects on the soft copy which are actually film defects on the hard copies. The five radiologists did not see anything else of clinical importance on the soft copy that they did not see on the hard copy.

Table 2.1 Questionnaire Responses of Radiologist 1

Radiologist 1	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
ID #	H/S	H/S	H/S	H/S	H/S	H/S	H/S	Y/N	Y/N
1	H	H					H	N	N
2	H	H	H	H			H	N	N
3	H	H	H	H			H	N	N
4			H	H			H	N	N
5	H	H	H	H	H	H	H	N	Y
6	H	H			H	H	H	N	N
7	H	H					H	Y	N
8	H	H					H	Y	N
9	H	H	H	H	H	H	H	Y	N
10	H	H					H	Y	N
11	H	H	H	H			H	Y	N
12			H	H			H	Y	N
13					H	H	H	N	N
14	H	H	S	H			H	Y	N
15	H	H	H	H			H	N	N
16			H	H			H	Y	N
17	H	H	H	H			H	Y	N
18	H	H	H	H			H	N	N
19					H	H	H	N	N
20	H	H					H	Y	N
21	H	H					H	Y	N
22	H	H	H	H			H	Y	N
23	H	H					H	Y	N
24			H	H			H	N	N
25	H	H	H	H			H	N	N
26			H	H			H	Y	N
27	H	H	H	H			H	Y	N
28			H	H			H	N	N
29			S	H			H	N	N
30			H	H			H	N	N
31	H	H	H	H	H	H	H	N	N
32			H	H			H	N	N
33			H	S			S	N	Y
34	H	H					H	N	N
35			S	H			H	N	N
36	H	H					H	N	N
37	H	H					H	Y	N
38	H	H	H	H			H	N	N
39					S	H	neither	N	N
40	H	H					H	N	N
41	H	H					H	N	N
42	H	H					H	N	N
43			S	H	H	H	H	N	N
44							H	N	N
45	H	H					H	N	N
46	H	H					H	N	N
47	H	H					H	N	N
48	H	H	S	H			H	N	N
49	H	H			S	H	H	N	N
50	H	H	S	H			H	Y	N

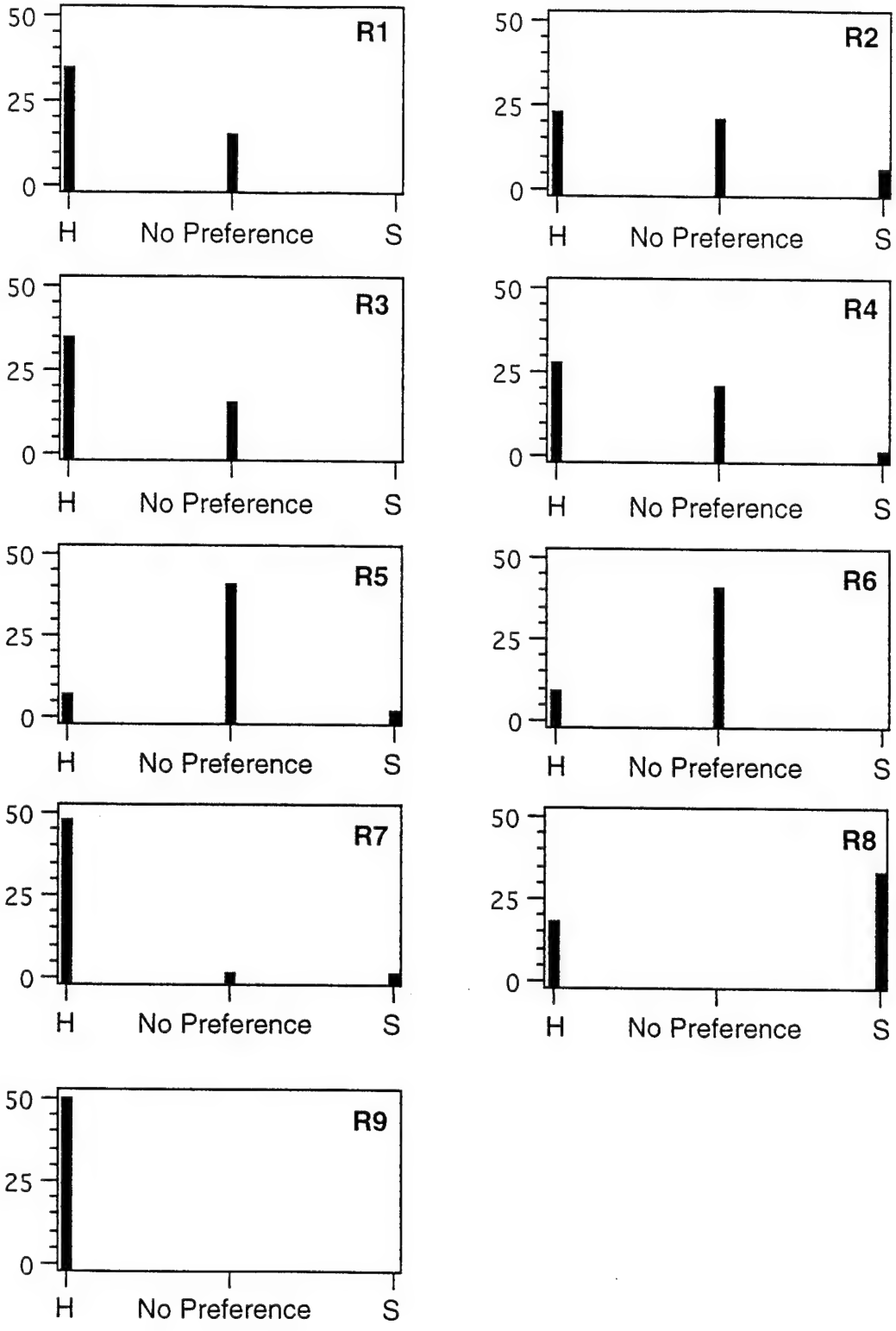


Figure 3.1 Questionnaire Response of Radiologist 1.

Table 2.2 Questionnaire Responses of Radiologist 1

Radiologist 2	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
ID #	H/S	H/S	H/S	H/S	H/S	H/S	H/S	Y/N	Y/N
1	H	H	H/S	H/S	H/S	H/S	H	Y	N
2	H	H	H/S	H/S	H/S	H/S	H	N	N
3	H	H	H/S	H/S	H/S	H/S	H	Y	N
4	H/S	H	H/S	neither	S	S	S	Y	N
5	H	H	S	S	S	S	S	N	N
6	H	H	H/S	neither	S	neither	neither	Y	N
7	H	H	H/S	neither	H/S	neither	H	Y	N
8	H	H	neither	neither	neither	neither	H	Y	N
9	H	H	S	neither	S	neither	H	Y	N
10	H	H	S	neither	neither	neither	H	Y	N
11	H	H	H/S	H/S	H/S	H/S	H	Y	N
12	H	H	H/S	neither	H/S	neither	neither	Y	N
13	H	H	S	S	S	S	S	Y	N
14	H	H	neither	neither	neither	neither	H	Y	N
15	H	H	H/S	neither	H/S	neither	H	Y	N
16	H	H	H	H	H	H	H	Y	N
17	H	H	H/S	neither	H/S	neither	H	Y	N
18	H	H	H/S	H/S	H/S	H/S	H	Y	N
19	H	H	neither	neither	S	neither	H	Y	N
20	H	H	neither	neither	neither	neither	H	Y	N
21	H	H	neither	neither	neither	neither	H	Y	N
22	H	H	H/S	neither	H/S	neither	H	Y	N
23	H	H	H/S	neither	S	neither	H	Y	N
24	neither	neither	H/S	neither	S	neither	H	N	N
25	H	H	H	neither	H	neither	H	Y	N
26	neither	neither	H/S	neither	H/S	neither	neither	N	N
27	H	H	H/S	neither	H/S	neither	H	Y	N
28	H	H	S	neither	S	neither	neither	Y	N
29	H	H	H/S	neither	H/S	neither	H	Y	N
30	H	H	H/S	H/S	H/S	H/S	H	Y	N
31	H	H	S	S	S	S	S	Y	N
32	H	H	H/S	neither	H/S	neither	H	Y	N
33	H	H	S	S	S	S	S	Y	N
34	H	H	S	neither	S	neither	no	Y	N
35	H	H	H/S	S	H/S	S	S	N	N
36	H	H	H	H	H	H	H	Y	N
37	H	H	neither	neither	neither	neither	H	Y	N
38	H	H	S	S	S	S	both	Y	N
39	H	H	H/S	neither	H/S	neither	H	Y	N
40	H	H	H/S	neither	H/S	neither	H	Y	N
41	H	H	H/S	S	H/S	S	S	Y	N
42	H	H	H	H	H	H	H	Y	N
43	H	H	H	H	H	H	H	Y	N
44	H	H	H/S	neither	H/S	neither	H	Y	N
45	H	H	H/S	neither	H/S	neither	H	Y	N
46	H	H	H/S	neither	H/S	neither	H	Y	N
47	H	H	neither	neither	neither	neither	H	Y	N
48	H	H	neither	neither	neither	neither	H	Y	N
49	H	H	S	S	S	S	S	Y	N
50	H	H	H/S	neither	H/S	neither	H	Y	N

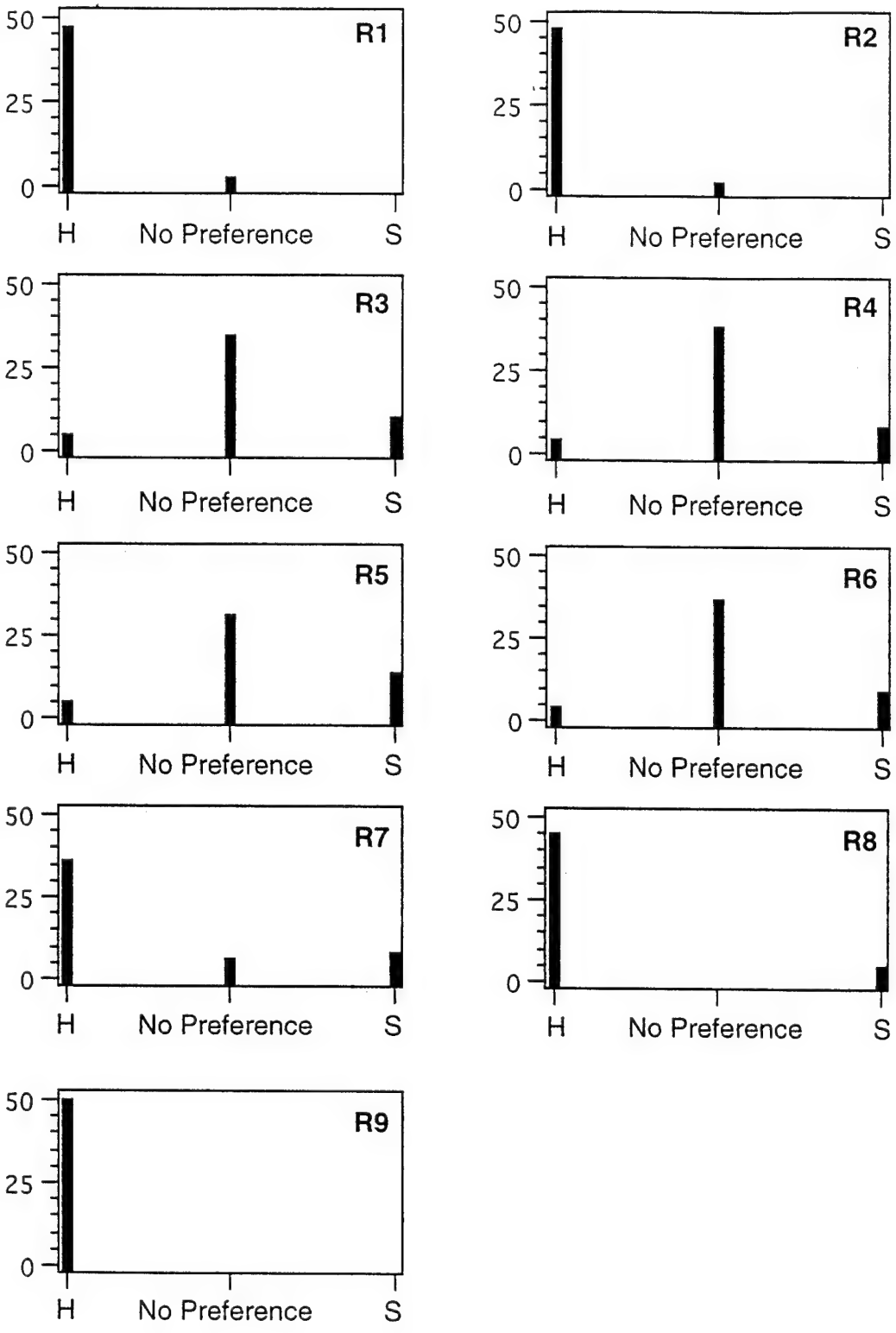


Figure 3.2 Questionnaire Response of Radiologist 2.

Table 2.3 Questionnaire Responses of Radiologist 3

Radiologist 3	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
ID #	H/S	H/S	H/S	H/S	H/S	H/S	H/S	Y/N	Y/N
1	H	H	H	H	H	H	H	Y	N
2	H	H	H	H	H	H	H	Y	N
3	H	H	H	H	H	H	H	N	N
4	H	H	H	H	H	H	H	Y	N
5	H	H	H	H	H	H	H	Y	N
6	H	H	H	H	H	H	H	N	N
7	H	H			H	H	H	Y	N
8	H	H			H	H	H	Y	N
9	H	H			H	H	H	Y	N
10	H	H	H	H			H	Y	N
11	H	H	H	H	H	H	H	Y	N
12			H	H	H	H	H	Y	N
13	H	H	H	H	H	H	H	Y	N
14	H	H	H	H	H	H	H	Y	N
15	H	H	H	H			H	Y	N
16	H	H			H	H	H	Y	N
17	H	H	H	H			H	Y	N
18	H	H	H	H	H	H	H	Y	N
19	H	H			H	H	H	Y	N
20	H	H			H	H	H	Y	N
21	H	H			H	H	H	Y	N
22	H	H			H	H	H	Y	N
23	H	H	H	H	H	H	H	Y	N
24	H	H	H	H			H	Y	N
25	H	H	H	H			H	N	N
26	H	H	H	H	H	H	H	N	N
27	H	H	H	H	H	H	H	N	N
28	H	H	H	H	H	H	H	Y	N
29			H	H			H	Y	N
30			H	H			H	N	N
31	H	H	H	H	H	H	H	Y	N
32	H	H	H	H			H	N	N
33	H	H	H	H	H	H	H	N	N
34	H	H					H	Y	N
35	H	H	H	H			H	N	N
36	H	H	H	H			H	Y	N
37	H	H			H	H	H	Y	N
38	H	H	H	H	H	H	H	Y	N
39	H	H			H	H	H	N	N
40	H	H	H	H			H	Y	N
41	H	H	H	H	H	H	H	Y	N
42	H	H	H	H	H	H	H	N	N
43	H	H	H	H	H	H	H	Y	N
44					H	H	H	N	N
45	H	H	H	H	H	H	H	Y	N
46	H	H	H	H	H	H	H	Y	N
47	H	H					H	Y	N
48	H	H			H	H	H	Y	N
49	H	H	H	H			H	N	N
50	H	H			H	H	H	N	N

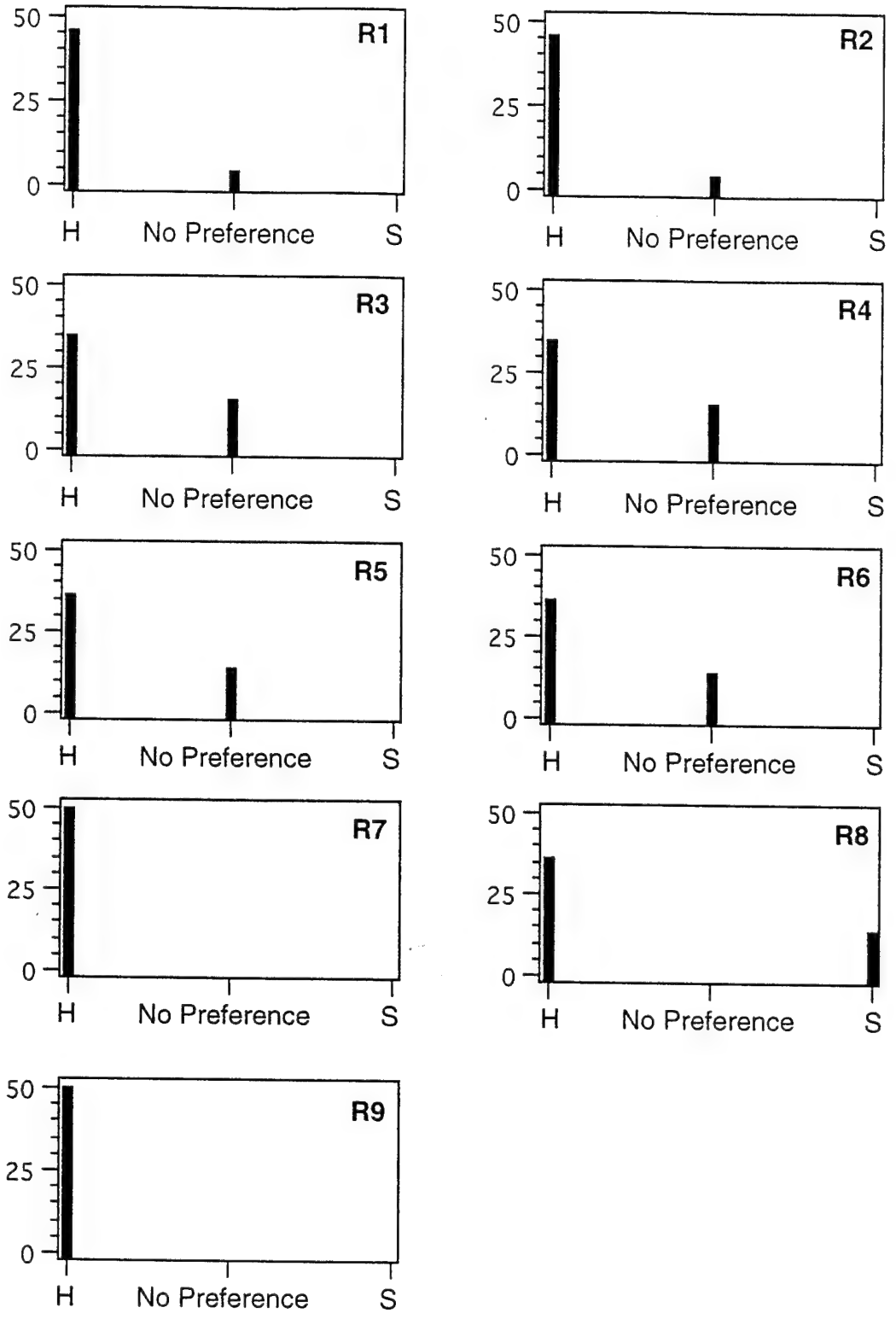


Figure 3.3 Questionnaire Response of Radiologist 3.

Table 2.4 Questionnaire Responses of Radiologist 4

Radiologist 4	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
ID #	H/S	H/S	H/S	H/S	H/S	H/S	H/S	Y/N	Y/N
1	H	H	H/S	H/S	H/S	H	H	Y	N
2	H	H	H	H	H/S	H/S	H	N	N
3	H/S	H/S	H/S	H			H	N	N
4	H	H	H/S	H/S			H	N	N
5	H/S	H/S	H/S	H/S			H	N	N
6	H/S	H/S			H/S	H/S	H	N	N
7	H/S	H/S			H/S	H/S	H	N	N
8	H/S	H/S			H/S	H/S	H	N	N
9	H	H	H	H	H	H	H	Y	N
10	H	H					H	N	N
11	H	H	H/S	H/S	H/S	H	H	Y	N
12	H	H	H	H			H	N	N
13			H/S	H			H	N	N
14	H	H	H/S	H			H	Y	N
15			H/S	H/S			H	N	N
16	H	H	H	H			H	Y	N
17	H	H					H	Y	N
18	H	H	H/S	H/S			H	Y	N
19	H	H			H/S	H	H	N	N
20	H/S	H					H	N	N
21	H	H			H/S	H/S	H	Y	N
22	H	H			H/S	H	H	Y	N
23	H	H					H	Y	N
24			H/S	H/S			H	N	N
25	H/S	H/S	H/S	H/S			H	N	N
26			H/S	H			H	Y	N
27	H	H	H/S	H			H	Y	N
28	H	H	H/S	H/S	H/S	H/S	H	Y	N
29			H/S	H/S			H	N	N
30	H	H	H/S	H/S			H	N	N
31	H/S	H/S	H/S	H/S	H/S	H/S	H	N	N
32			H/S	H/S			H	N	N
33			H	H			H	Y	N
34	H	H/S					H	N	N
35	H/S	H/S	H/S	H/S			H	N	N
36	H	H					H	N	N
37	H	H			H	H	H	Y	N
38	H/S	H/S	H/S	H/S	H/S	H/S	H	N	N
39	H	H			H	H	H	Y	N
40	H	H			H/S	H/S	H	Y	N
41	H	H	H/S	H	H/S	H	H	Y	N
42	H	H	H/S	H/S	H/S	H/S	H	Y	N
43	H	H/S	H/S	H/S	H/S	H/S	H	N	N
44							H	Y	N
45	H	H	H/S	H/S			H	Y	N
46	H/S	H/S	H/S	H/S			H	N	N
47	H/S	H/S					H	N	N
48	H	H	H	H	H/S	H/S	H	N	N
49	H	H			H/S	H/S	H	Y	N
50	H	H	H/S	H/S			H	Y	N

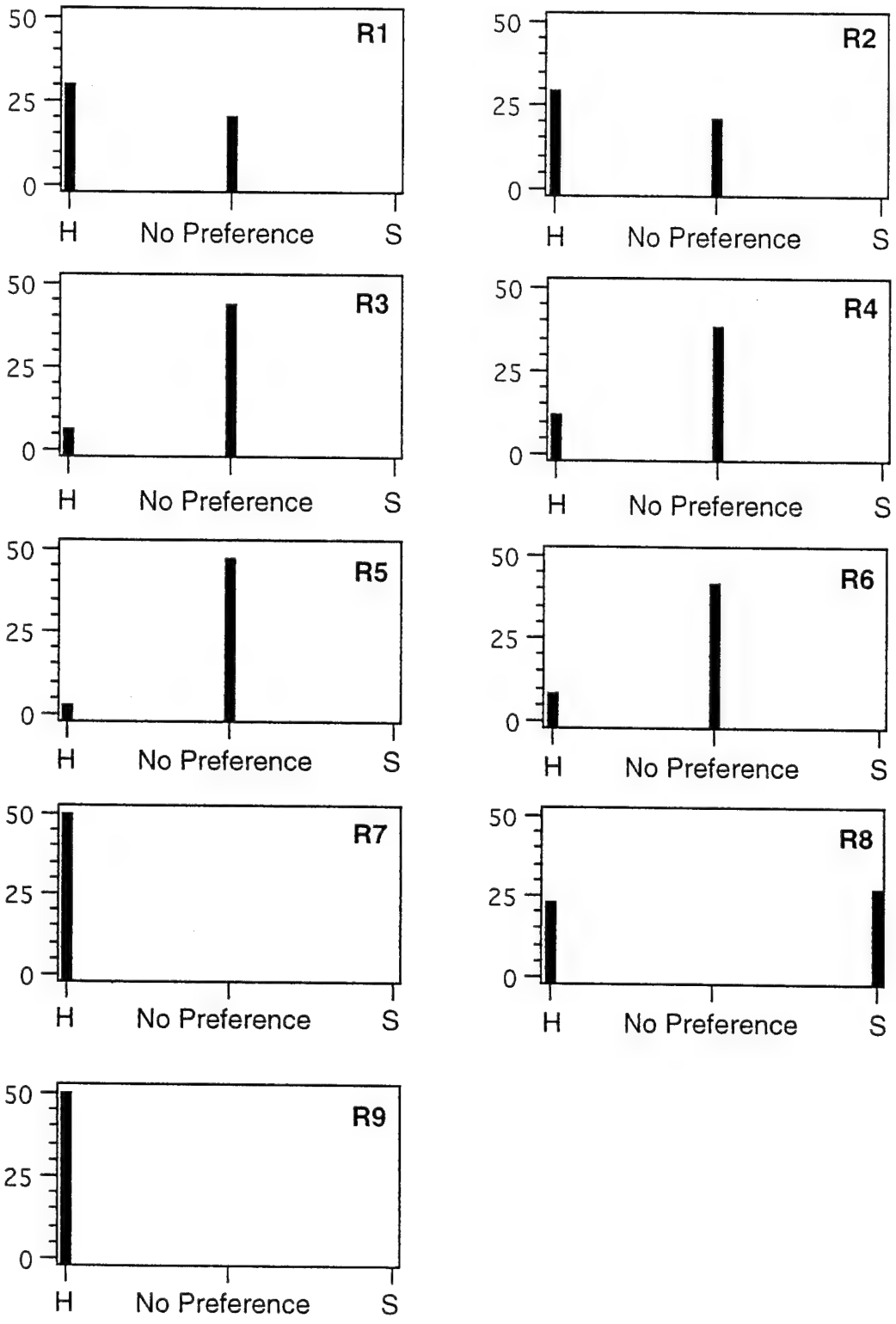


Figure 3.4 Questionnaire Response of Radiologist 4.

Table 2.5 Questionnaire Response of Radiologist 5

Radiologist 5	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9
ID #	H/S	H/S	H/S	H/S	H/S	H/S	H/S	Y/N	Y/N
1	H	H	H	H	H	H	H	Y	N
2	H	H	H	H			H	N	N
3			H	H	H	H	H	N	N
4	H	H	H	H	H	H	H	N	N
5	H	H	H	H			H	N	N
6	H	H	H	H			H	N	N
7	H	H	H	H	H	H	H	Y	N
8	H	H					H	Y	N
9					H	H	H	N	N
10	H	H	H	H			H	N	N
11	H	H	H	H	H	H	H	N	N
12							H	N	N
13							H	N	N
14	H	H	H	H	H	H	H	Y	N
15	H	H					H	N	N
16	H	H	H	H			H	Y	N
17	H	H	H	H			H	N	N
18	H	H					H	Y	N
19	H	H					H	N	N
20	H	H	H	H	H	H	H	N	N
21	H	H	H	H	H	H	H	Y	N
22	H	H	H	H	H	H	H	Y	N
23	H	H	H	H	H	H	H	Y	N
24							H	N	N
25			H	H	H	H	H	N	N
26			H	H	H	H	H	N	N
27	H	H					H	Y	N
28	H	H					H	Y	N
29							neither	N	N
30							neither	N	N
31			H	H			H	Y	N
32			H	H			H	N	N
33							neither	N	N
34	H	H					H	N	N
35	H	H					H	Y	N
36	H	H					H	Y	N
37	H	H			H	H	H	Y	N
38	H	H	H	H			H	Y	N
39							neither	N	N
40	H	H					H	Y	N
41	H	H	H	H			H	N	N
42	H	H					H	Y	N
43							neither	N	N
44			H	H	H	H	H	N	N
45	H	H	H	H	H	H	H	N	N
46	H	H					H	N	N
47							H	N	N
48	H	H					H	Y	N
49	H	H	H	H			H	N	N
50	H	H					H	Y	N

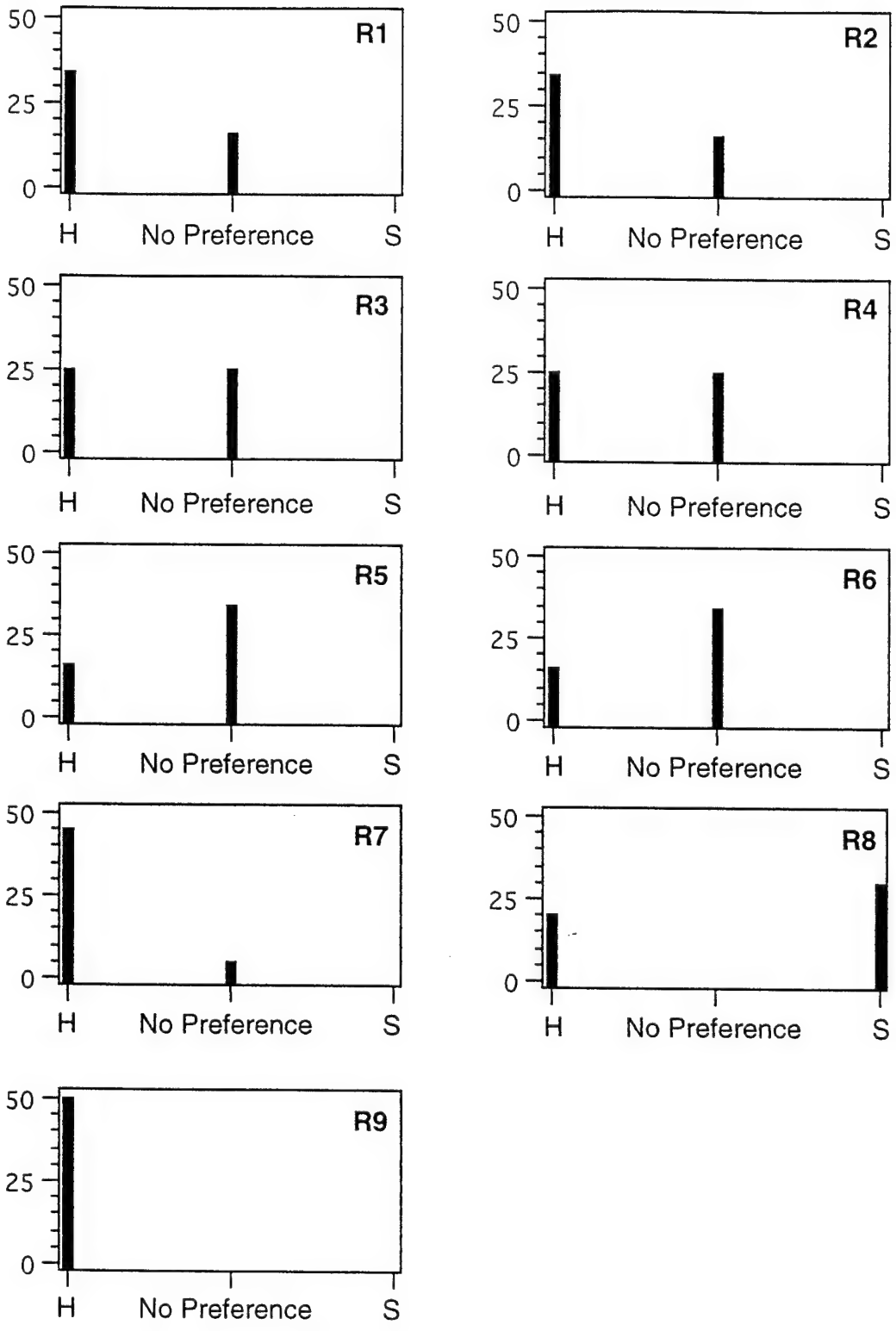


Figure 3.5 Questionnaire Response of Radiologist 5.

5.2. Comments of the Five Radiologists

Dr. Hayes's Comments:
- Prefer the hard copy to soft copy.
- Microcalcifications were difficult to see on soft copies unless the contrast was increased considerably, however, at that time the remainder of the breast is too dark.
- Microcalcifications can not only be identified more easily on hard copy (10 line pairs), they can also be better defined on hard copy as to benign vs. malignant.
- Due to the magnification with soft copies, masses sometimes are more easily detected and better characterized with soft copies.
- On soft copies it was difficult to evaluate the skin without changes in density.
- By changing density on soft copy skin retraction can be better detected than on hard copy without "hot light".
- Can better define number and sizes of calcifications and detect more scattered microcalcifications on hard copy.
- Can not determine adequate number of microcalcifications on soft copy. Microcalcifications are better delineated on hard copy. However, because of the lower resolution on soft copy, some microcalcifications are smudged and can not be seen on soft copy.
- Some easily identified artifacts on the hard copy almost look like microcalcifications on the soft copy. Artifacts are more clearly defined on hard copy.

Dr. Hogge's Comments:
- Calcifications are lost on soft copies in areas of dense tissue - this is a serious limitation.
- Masses are better depicted on soft copies in parts with fatty breasts, but not in dense breasts.

Dr. Freedman's Comments:
- Soft copy naturally makes it harder to see microcalcifications and sometimes they can not be seen at all.
- Masses and asymmetry density are lower central on soft copies and therefore harder to search.

Dr. Green's Comments:
- Manipulation of the window-and-level took time and diverted vision and attention away from the image being diagnosed.
- Some images, especially those containing dense tissues, needed to be enhanced dramatically in the contrast, however, the information in other breast areas is lost.

Dr. Zuurbier's Comments:
- In general, the soft copy images have a "gauze-y" veil-like effect (and resolution).
- Soft copy seems to increase the perception of normal soft tissue structures as abnormal.
- Soft copy loses faint but important microcalcifications in dense tissue.
- Hard copy provides better sense of the contrast of whole image, normal and abnormal soft tissues.
- See detail of dense soft tissue better on hard copy.

6. CONCLUSIONS

• **Image Spatial Resolution** - Our study results showed that, in general, the five radiologists preferred hard copy to soft copy screen films. It also showed that the disease patterns are better characterized on hard copy than on soft copy SF. Because of the spatial resolution of the soft copy, some subtle microcalcifications in the dense tissue area are not well characterized and become difficult to detect. Furthermore, some obvious film defects on the films become microcalcification-like on the soft copy where spatial resolution and contrast become lower than those on the hard copy. Specifically, the screen film hard copy has a spatial resolution of approximately 10 line pairs per millimeter while the digitized 100 μm SF (i.e., soft copy) has only about 5 line pairs per millimeter. The results indicate that high spatial resolution is important in the identification of some subtle and faint microcalcifications in the dense breast area. Direction digitization of screen film at 100 μm and without other image enhancement is not adequate to retain the important clinical information of the microcalcifications, especially those are small and subtle microcalcifications which lie in the dense breast areas. The radiologists experience and training in reading soft copy may have some effects on the study results.

• **Classification of Benign and Malignant Diseases** - The classification of benign and malignant disease patterns, such as microcalcifications and masses, presented a very challenging task for the radiologists. Our study results showed that the five radiologists achieved average 50% accuracy in the classification of benign and malignant disease patterns. The five radiologists found single or multiple disease patterns in all 50 cases (see also the "MAMMO FINDINGS" in Table 1), however, only 25 cases were biopsy proven cases. The 50% accuracy on cancer case was measured no matter what the disease - microcalcification, mass, or architecture distortion. The study of using artificial neural network (ANN) and computer-aided diagnosis (CADx) to classify benign and malignant microcalcifications is currently under intensive investigation at ISIS Center.

• **Display Workstation** - The Vicom display workstation which provides 8 bit (256 gray levels) display is not sufficient to the contrast information on the films as perceived by the radiologists. The contrast and intensity of the abnormal soft tissues as opposed to that of normal soft tissues are better perceived on the hard copy; the abnormal and normal soft tissues of the soft copy have similar contrast and intensity when displayed on the monitors. In some cases, masses and architecture asymmetry were easier to detect on the soft copy partly because of the magnification when displayed on the display monitors. However, the high contrast on the hard copy make the masses better characterized than on soft copy.

• **Periodic Maintenance and Quality Control** - Periodic maintenance of film digitizer and QC on Fuji CR9000 and display monitors are necessary in digital mammography of the MDIS environment. We are in the process of acquiring a multi-format pattern generator and a comprehensive display evaluation system for QC on high resolution display monitors.

• **On-going Researches** - The results of this study indicate that, based on our current experimental setting, soft copy display is not good enough to be clinically useful. However,

improvement and optimization of display equipment and advanced image processing, such as the unsharp masking technique provided by Fuji CR systems, may make soft copy display more clinically useful. Two possible research directions: one is to apply image processing to enhance microcalcifications especially in the dense breast areas of 100 micron images, the other is to use 50 mm images and a higher gray level (10 or 12 bit) instead of an 8 bit display monitor.

- The dispay of the full image dat of a mammogram digitized at 50 micron resolution (4096 pixels × 5120 lines × 12 bits) may require roaming of the image on the 2048 pixels × 2560 lines display monitor. The potential effects, such as the diversion of vision and attention away from the region-of-interest being viewed, caused by roaming and other image manipulations need to be further investigated.
- We have developed a region-based image processing technique to enhance the visibility of subtle microcalcifications in the dense tissues. The comparative study of SF and the processed 100 micron SF images is currently under development.

7. ADDENDA

7.1. Acronym / Symbol Definition

ACR -	American College of Radiology
ACR-NEMA -	ACR-National Electrical Manufacturers Association
CDMAM -	Contrast detail mammogram-phanton
CIRS -	Computerized Imaging Reference Systems
CR -	Computed radiography
DASM -	Data acquisition and system management
GUMC -	Georgetown University Medical Center
LCC -	Left cranio caudal
LMLO -	Left mediolateral oblique
MDIS -	Military diagnostic imaging systems
QC -	Quality control
RCC -	Right cranio caudal
RMLO -	Right mediolateral oblique
SCIB -	Second channel interface board
SCSI -	Small computer system interface
SF -	Screen film
SMPTE -	Society of motion picture and television engineers

7.2. References

[1] Lumisys, *Lumiscan Service Manual: Model 100/150/200.* Sunnyvale, CA 94086, 1994.

[2] C. E. Metz, "Some practical issues of experimental design and data analysis in radiological ROC studies," *Investigative Radiology*, vol. 24, pp. 234-245, 1989.

IMAGE PROCESSING IN DIGITAL MAMMOGRAPHY

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OVERVIEW

INTRODUCTION

Digital mammography is likely to replace conventional mammography within a few years. In anticipation of this, our group has been exploring the implications of image processing in digital mammography. Some of our findings are reported here.

INITIAL STATUS

Initial investigations of a commercially available full breast digital mammography system demonstrated that, when evaluated on phantoms, the detection of small faint objects was less than with conventional screen film mammography (Chart 1).

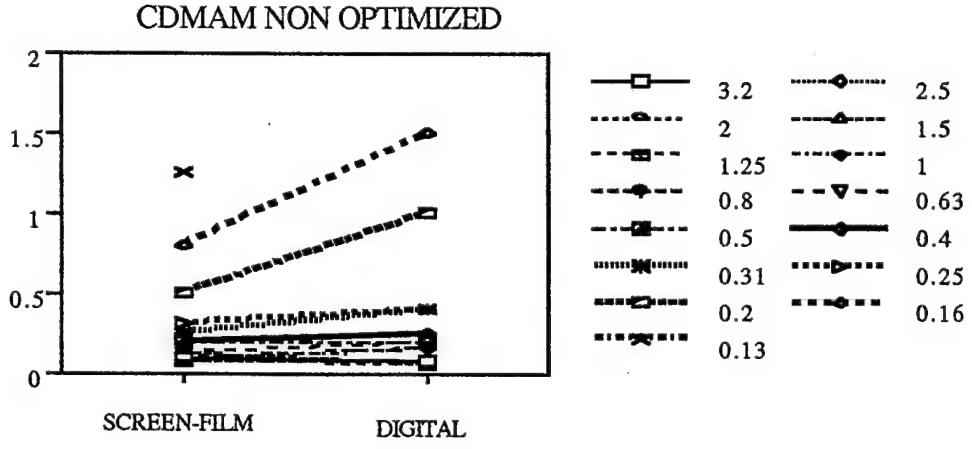


Chart 1: This chart reports a comparison between screen film (SF) mammography and storage phosphor (SR) digital mammography using the image processing settings provided by the manufacturer. For all smaller objects, the screen film system performed better. (The Y axis represents the minimal thickness at which an object could be identified, each line represents a small gold disk of decreasing diameter. A lower position on the chart indicates better performance.) (CDMAM Phantom, Nuclear Associates). Tests of the RMI #156 and CIRS phantom confirmed the initial inferior performance of the digital system.

0-8194-1459-X/94/$6.00

Figure 1: an image of the CDMAM Phantom.

Conversely, using experimental techniques, it is possible to demonstrate all objects of the phantom used for ACR accreditation. This experimental system can only image part of the breast and produces an image with obvious artifacts. (Figure 2)

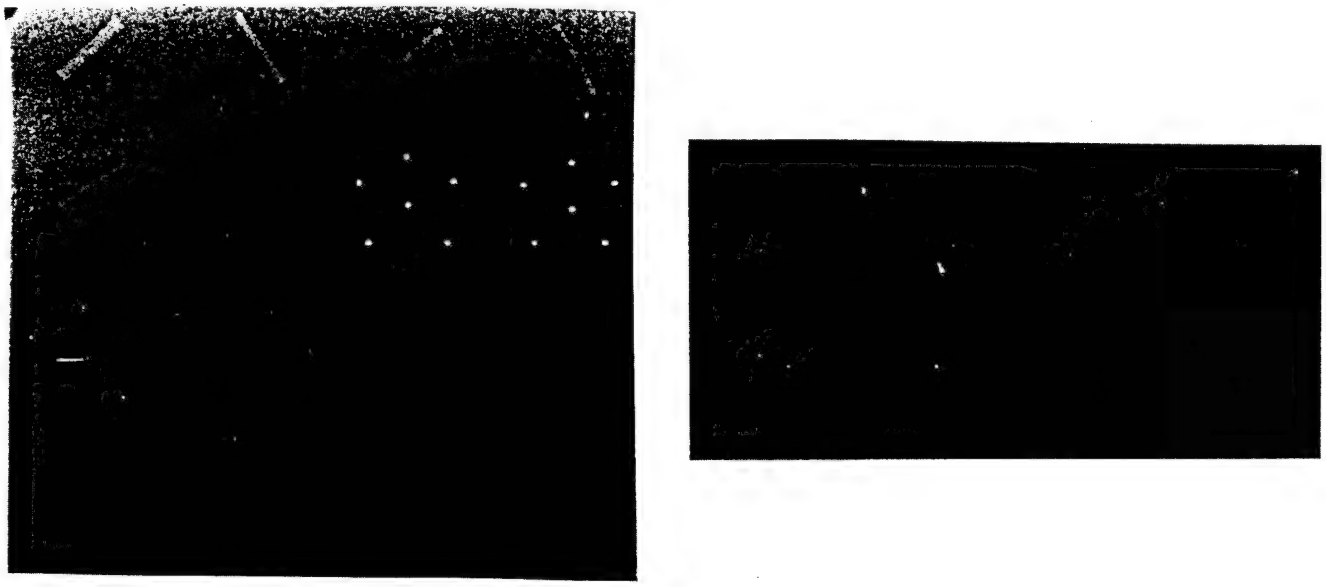


Figure 2: Digital radiograph of complete phantom (wax insert and plastic case) used for ACR accreditation (RMI #156). All objects on the phantom are visible. A magnified view of the same image shows the smallest two groups of "calcifications. This system can only image part of the breast.

IMAGE PROCESSING OPTIMIZATION PROCEDURE

A series of 3 dimensional response surfaces were obtained by processing images of the RMI, CDMAM, and CIRS phantoms. The following factors were considered: optical density, contrast, rotation center for contrast adjustment, spatial frequency filtering with different kernel sizes, spatial frequency emphasis, mAs, KVP, magnification, 2 types of phosphor plates, and focal spot size. These 10 different factors interact to varying degrees. Only selected pairs have been evaluated. In addition, the effects of 4 different effective pixel sizes were evaluated. Once improved images were found using these phantoms, the same settings were tested on several digitally acquired and electronically stored mammograms. Those image processing combined settings that resulted in unacceptably distorted images of the breast were rejected.

Optimization of a single factor was not sufficient to result in full potential information. Multiparameter, non-linear optimization was necessary and was roughly approximated by varying factors in pairs and substituting best settings of these factors in the optimization procedure of the other factors.

CURRENT STATUS

Based on the optimization procedure, a graph using the CDMAM phantom now demonstrates that using the commercially available full breast phosphor plate system, that for each object size, both systems detected or failed to detect objects of the same diameter and same minimal thickness. (Chart 2)

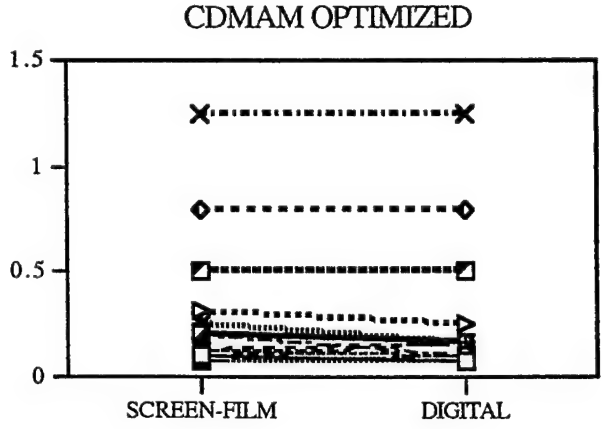


Chart 2: This chart demonstrates that for each diameter object, that the screen film and storage phosphor systems perform essentially the same as demonstrated by the lines being horizontal.

This can be achieved with a mammographic image that is different than conventional mammography, but is considered acceptable in appearance. (Figure 3)

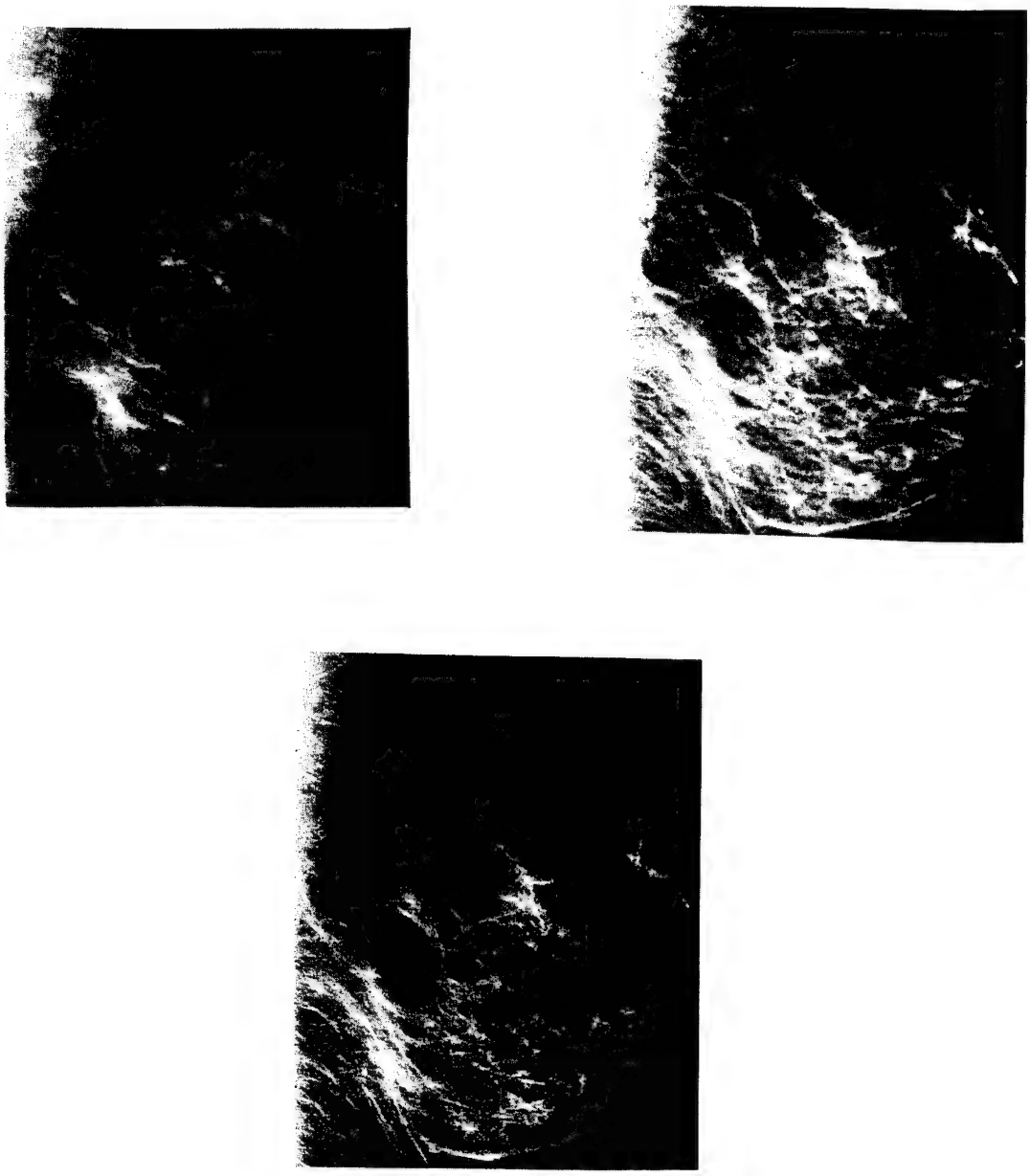


Figure 3: Mammogram of normal breast containing a few scattered microcalcifications. A. Conventional mammogram,
B. Digital mammogram. (GA=1.2, GT=G, GC=+0.3, RN=5, RT=P, RE=1). C. "Optimized" processed digital mammogram. (GA=1.9, GT=G, GC=+0.3, RN=9, RT=P, RE=5).

It was possible to devise algorithm settings that provided enhanced visualization of very small objects and of simulated masses when the digital image was compared to screen-film, but these processing settings resulting in human breast images that were considered unacceptably distorted. These distorted images might however prove to be clinically useful in selected problem cases when combined with other optimized images.

CONCLUSIONS

It is possible with a current digital mammography with proper image processing to equal the object detectability of a current screen-film mammography system, as measured on the RMI, CIRS and CDMAM phantoms and to produce a breast image that is likely to be acceptable to practicing radiologists.

BASIC CONCEPTS OF IMAGE PROCESSING:

This exhibit is intended to provide background information for understanding image processing in digital mammography.

RESOLUTION AND CONSPISCUITY:

The potential benefits from digital mammography would come from improved visualization of micro calcifications, thin linear structures and masses. The ability to detect objects depends on a combination of resolution and conspicuity. Resolution relates to the smallest sized object that can be seen. Conspiscuity refers to the detectabilty of an object as separate from its background by a human observer (how conspicuous it is) and is related to resolution, contrast, and viewing conditions.

THE USE OF PHANTOMS IN TESTS:

There are several mammography phantoms in use. These phantoms have different structures and their use reveals different aspects of image quality.

RESOLUTION:

Fundamental concepts:

REQUIRED PIXEL SIZE TO DETECT A SMALL OBJECT

A pixel is a picture element. Resolution and the pixel size necessary to detect a small object are not same. The maximal resolution of a picture divided into pixels, is the pixel size. The smallest detectable object is based on four factors: the size of the object, the size of the pixel, the position of the object in relation to the pixel and the relative radiodensity of the object compared to the background. Given adequate differences between the object and background density, the detection of a spherical calcium radiodensity object requires that the object and its penumbra be approximately $2\sqrt{2}$ times the size of the pixel. If the object is of greater radiodensity or is thicker, then smaller objects can be detected.

FILLING THE PIXEL:

If the pixel area is not filled, contrast is reduced.
The minimum detectable size is greater than the pixel size in most situations.

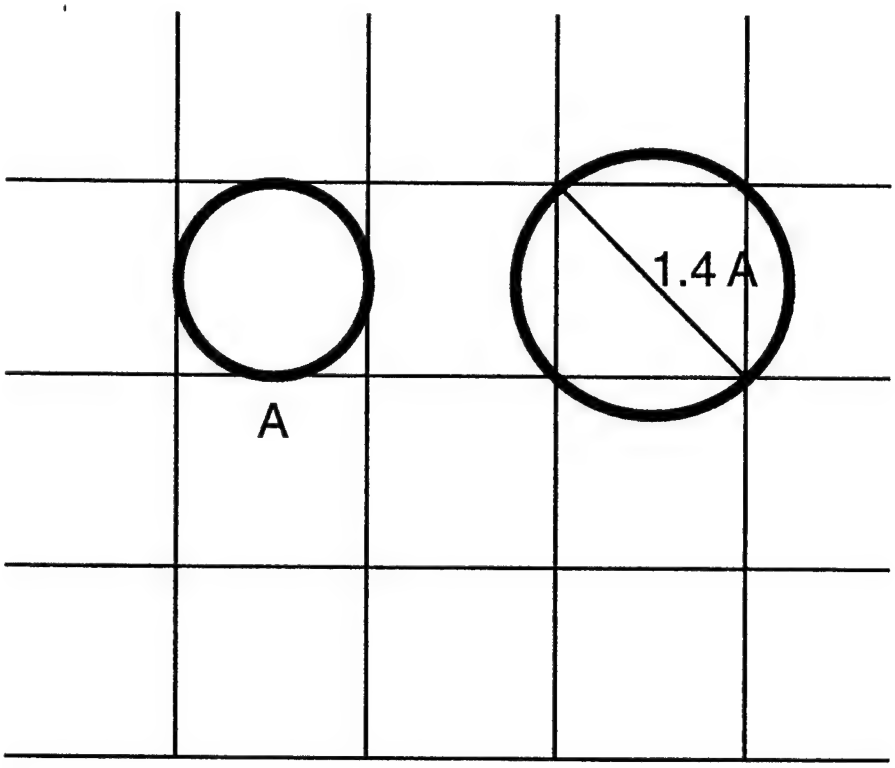


Figure 4: A sphere within a pixel has the same diameter as the pixel, but fills only 50% of a cubic voxel of the same size. Thus its radiodensity is only 1/2 of an object of similar thickness that completely fills the pixel. To fill a pixel of size A, need a sphere

If centered on pixel of size A
by Pythagorean Theorem: A $\sqrt{2}$.

EFFECT OF NOT FILLING PIXEL

Decreased contrast (similar to partial volume effect)

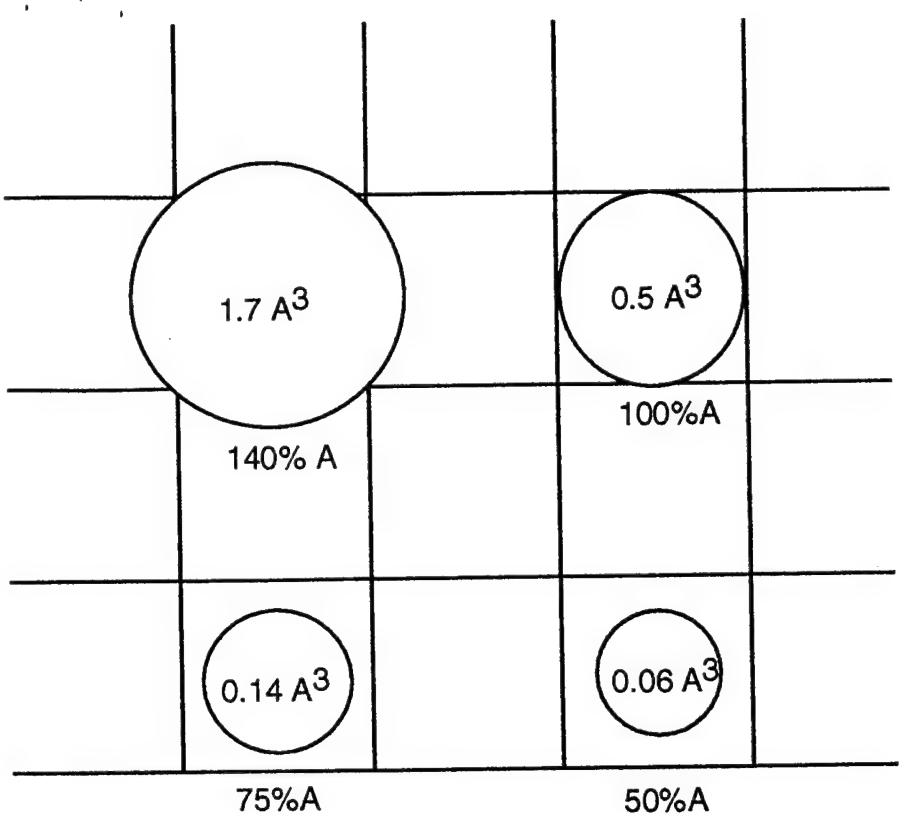


Figure 5: The volume of calcium projected in sphere of pixel size A with spheres of different sizes projected in center of pixel. (Based on solid geometry formulas.) The radiodensity projected on the pixel and averaged over the total area of the pixel rapidly decreases.

If an object is of increased radiodensity, then it can be smaller. Thus an object of 2 times the pixel size can be seen if it is twice as radiodense as an object seen when it is $2\sqrt{2}$ times the size of the pixel. This is demonstrable on the CDMAM phantom.

EFFECT IF OBJECT IS NOT CENTERED TO PIXEL

If calcium size is $\sqrt{2}$ A, minimum density will be 1/4 of that if the pixel is completely filled. (37% filled, but because of sphere only 1/4 of density). (Figure 6)

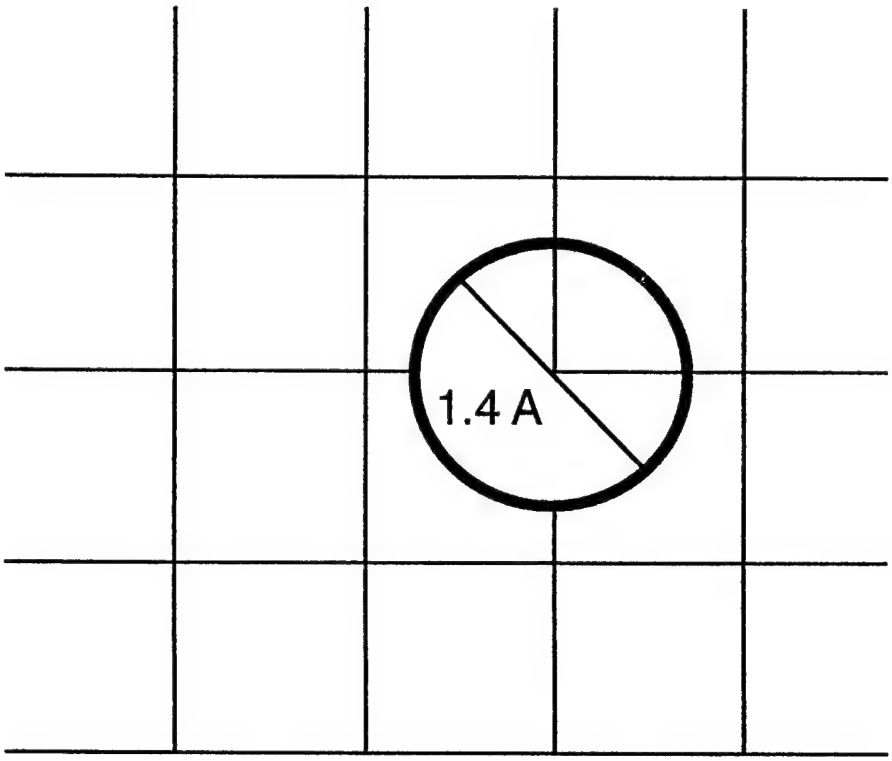


Figure 6: Drawing showing effect of maximal offset of $\sqrt{2}$ A sphere on area of pixel filled.

This is not of sufficient radiodensity to be detectable for spherical objects of calcium radiodensity.

If offset maximal amount (oblique)
need 2A $\sqrt{2}$ to be certain that one pixel is completely filled.

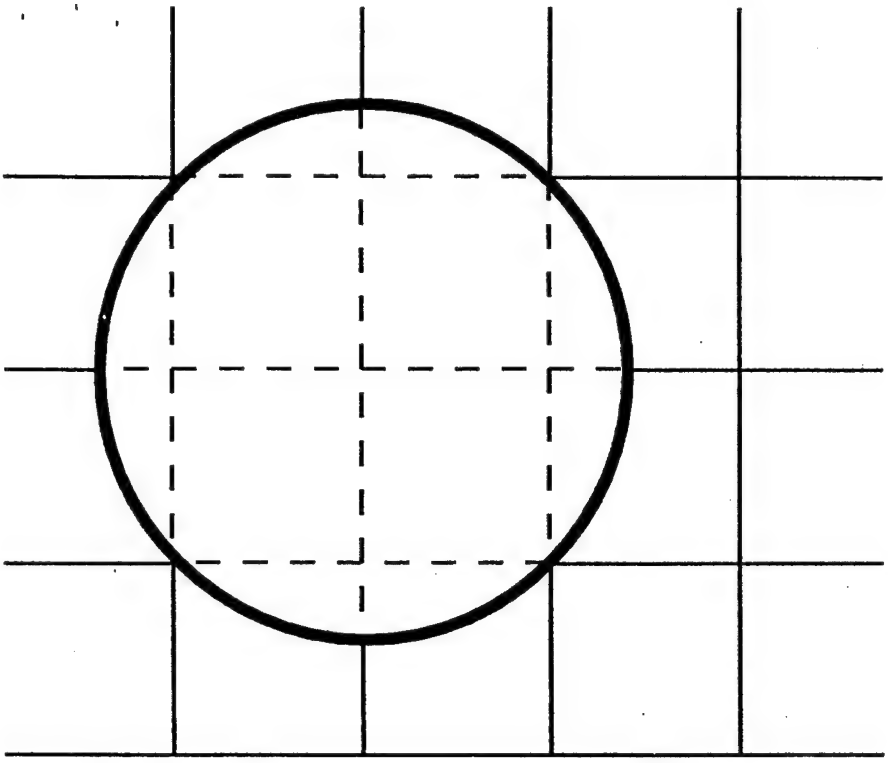


Figure 7: Drawing of sphere of diameter 2A $\sqrt{2}$ offset to corner of pixel.

Therefore, to consistently detect an object, one needs a 2A $\sqrt{2}$ sized object.

For a

320 micron object need 114 micron pixel
240 micron object need 85 micron pixel
160 micron object need 57 micron pixel

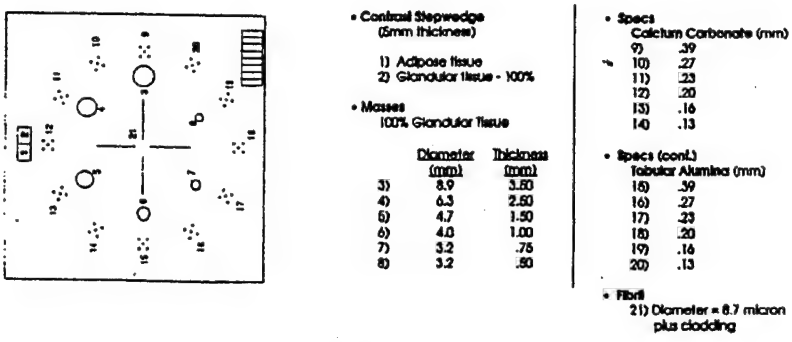
THE DIRECT HIT

Occasionally, a smaller object will be sufficiently superimposed on the center of a pixel so that it can be seen. This is a random, rather than a predictable occurrence.

FILLING THE PIXEL: EXPERIMENTAL EVIDENCE

We can just faintly see an object 160 microns plus penumbra with an 83 micron pixel. (from Figure 2). In that image, the object with penumbra is approximately 205 microns.

On the Fuji mammography system should be able to just see 290 micron object, but not the 200 micron object. In experiments, we can see 200 micron calcification in CIRS phantom. When actually measured on a screen film image, this 200 micron calcification actually measures 300 microns. Thus the value of 2 A $\sqrt{2}$ is a reasonable approximation. (Figure 8)



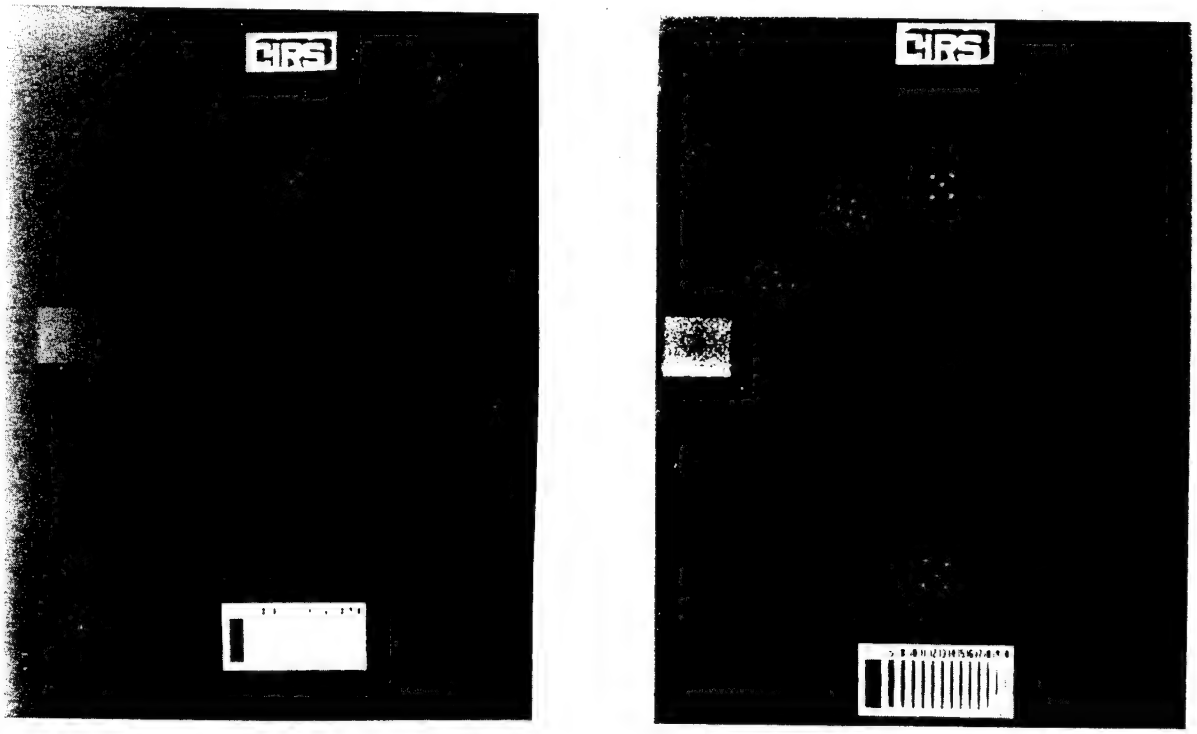


Figure 8: Storage phosphor image of CIRS phantom. Fuji HR-V plates. No magnification.

A: Drawing and measurements.

B: Screen-Film Radiograph.

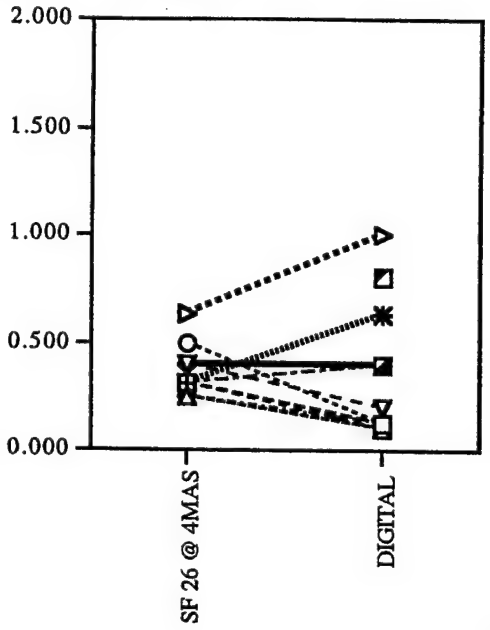
C: Storage Phosphor Radiograph (Fuji high resolution system with HR V plates).

FACTORS AFFECTING OPTICAL DENSITY AND CONTRAST:

Image processing can be used to change the optical density and contrast of an image. The relation of this to improved images through digital mammography is discussed below.

EXPOSURE, NOISE, AND CONSPISCUITY:

In screen film systems, underexposure results in light images that limit the visibility of objects. In phosphor plate images, because one can correct the optical density of the image, the decreased exposure results in increased noise that limits the visibility of objects. At exposure levels necessary for full information, both systems performed equivalently. (Chart 3 A and B.)



4

Chart 3A records a comparison at 4 mAs of screen film and digital CDMAM object. The screen film (SF) system performs better for some objects sizes and poorer for others when compared to the digital system The digital system system shows one object (0.2 mm) that is smaller than those seen with the screen film system.

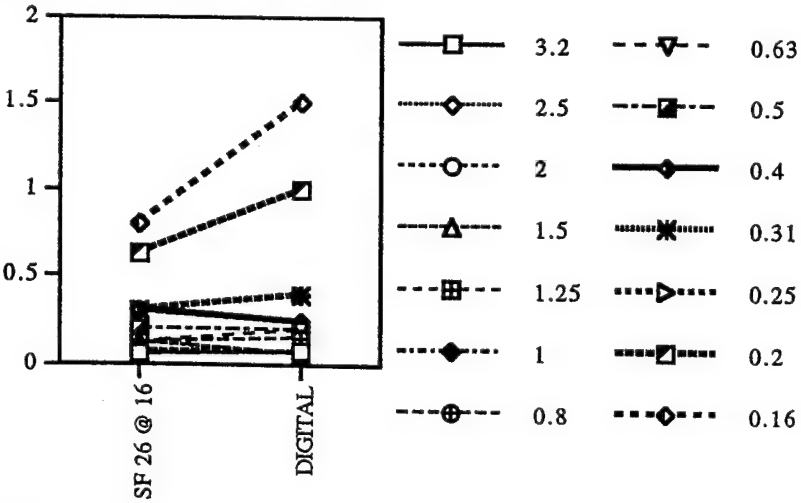


Chart 3 B demonstrates that at 16 mAs, the screen film system shows thinner objects for all object sizes than does the digital system. At 16 mAs, both systems showed the 0.16 mm diameter object. This object could not be seen with 4 or 6 mAs. The digital system was only partially optimized when this experiment was done.

Chart 4 This chart demonstrates the effect of increased exposure on detection of objects on the CDMAM phantom. A. Screen film. B. Storage phosphor

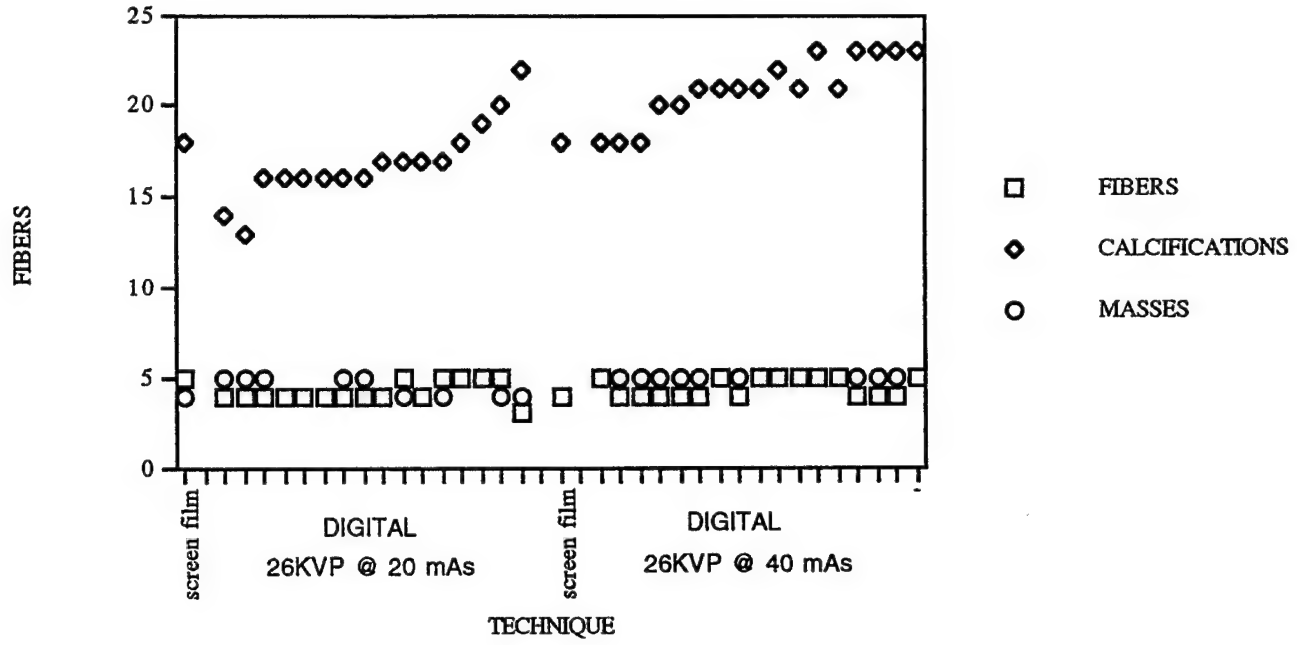


Chart 4. With the RMI phantom, increasing the exposure from 26 KVP at 20 mAs to 26 KVP at 40 mAs increases the detectability of calcifications in SR, but not with screen film. With the higher exposure, the SR system demonstrate more "calcifications" than the screen film system. Whether or not it is worthwhile to increase the exposure beyond that needed for SF mammography will depend on how useful finding these smaller calcifications proves to be.

OPTICAL DENSITY

Changing the optical density of an image can improve the visibility of objects that otherwise would fall in the toe or shoulder region of the image. Increasing the optical density in a region of calcifications by electronically shifting the calcifications to the steep portion of the contrast gradient can increase contrast and therefore visibility in the region of interest.

CONTRAST

Improving the contrast of the image can increase the detectability of objects.

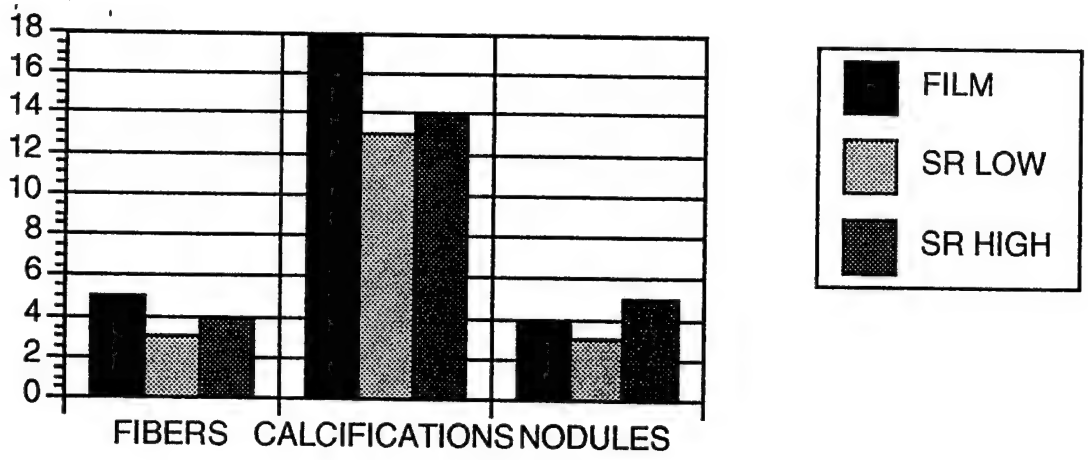
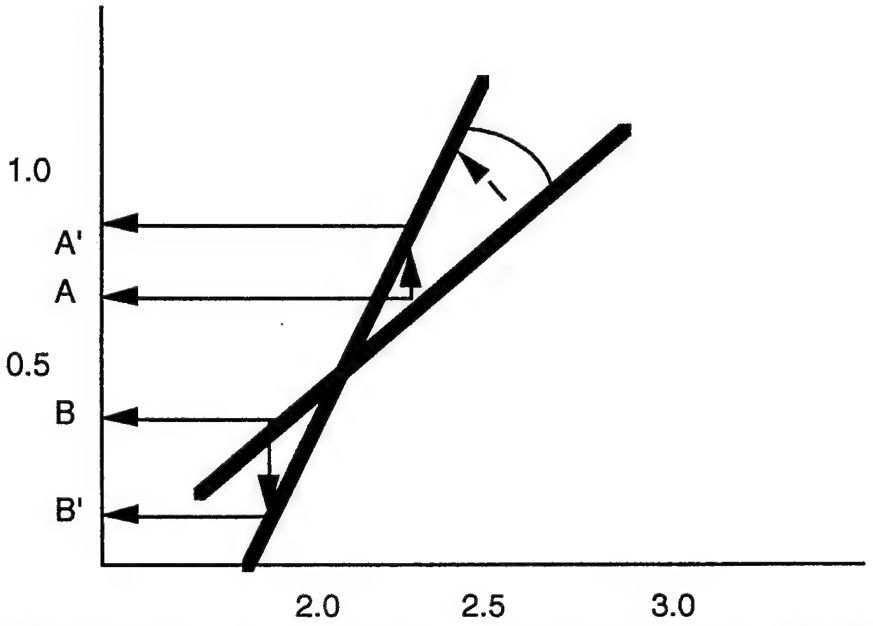


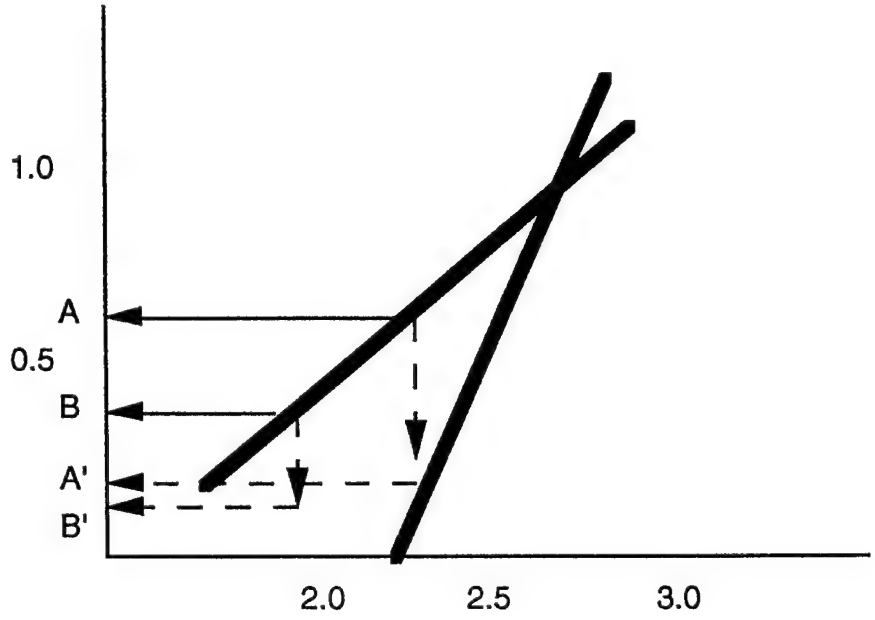
chart 5: This chart of objects detected on the RMI phantom demonstrates that the change from SR low contrast to SR high contrast increases the detectabililty of objects. High contrast makes the detection of masses to be greater than that of screen film mammography.

THE CENTER OF ROTATION

The contrast curve is rotated to increase the contrast. The center point for rotation is important in determining the contrast effect seen. If one wants to accentuate a calcium object against a background of higher optical density, the maximum separation will occur by placing the rotation center just above the OD of the calcium object. For any specific degree of contrast, this will allow the maximal visualization of the calcium, while minimizing the loss of information elsewhere in the image by creating too much contrast. The reason this occurs is that the system has limited ability to reflect low image optical densities and that for effective OD less than 0.3, further decreases have essentially no effect.



Thus if one increases the slope of the contrast curve and the center of rotation lies between the two objects to be separated, then the difference between the two points (the separation between A and B compared to A' and B') is increased.



If one places the center of rotation of the contrast curve on either side of both regions one is attempting to separate, and then increases the contrast, then the two points will lie closer together, i.e. have less contrast (change from A to B to the space between A' and B'). This is because the OD of the less dense object cannot decrease much below its initial level.

SPATIAL FREQUENCY

All images can be separated into mathematical formulae that represent the frequencies present in an image. These mathematical formulae can be used to reconstruct the image as it was. One can also use image processing to change the emphasis of different spatial frequencies in an image. One can choose ranges of frequencies to emphasize or de-emphasize. This processing can make information more visible or can conceal information.

Kernel size:

One common method for changing the emphasis given different spatial frequencies in an image is to do a convolution where the information is multiplied by a group of numbers that are selected to affect certain spatial frequencies. The kernel size refers to the size of the group of numbers used as the multiplier. In general, the smaller the kernel, the greater the emphasis given to smaller objects, the larger the kernel, the greater the emphasis given to larger objects.

The use of small kernels emphasizes sharp margins and can be called edge enhancement. The use of large kernels de-emphasizes sharp margins and can be called smoothing or noise reduction.

Using small kernels emphasizes the visibility of noise in an image. Use of large kernels decreases the sharp edges that aid in the detection of micro calcifications.

The effect of changes in kernel size and spatial frequency emphasis:

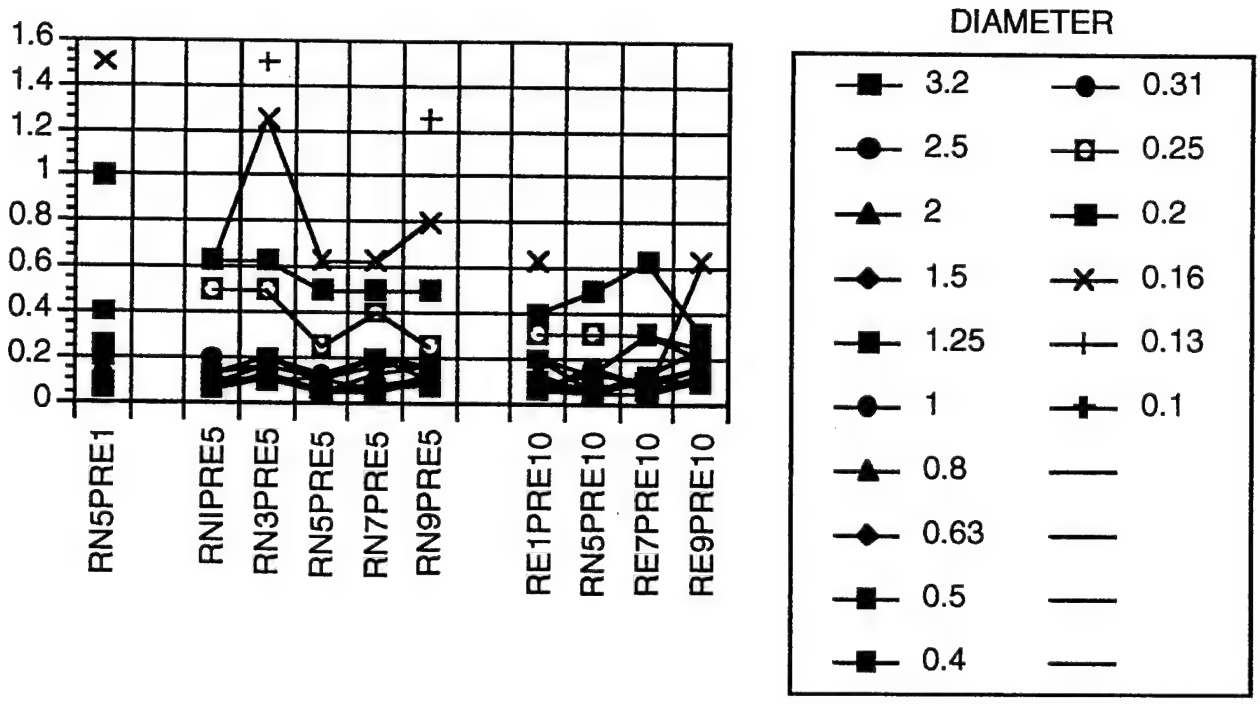
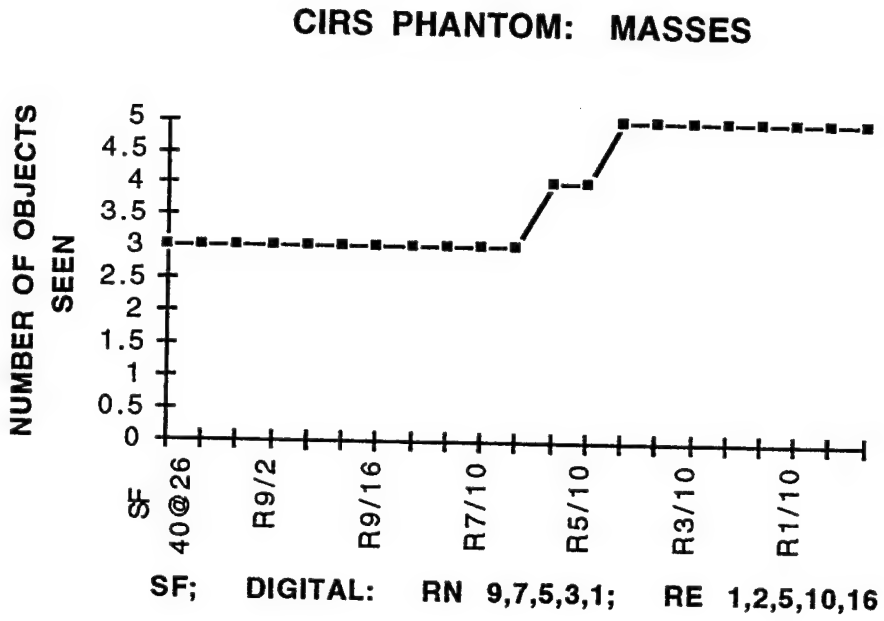


CHART 6: The effect of different degrees of emphasis (RE =1,5,10) for selected kernel sizes (RN = 1,3,5,7,9). Increasing the emphasis results in thinner objects being seen at all sizes. At the smallest kernel size (RN = 9), the high emphasis image increased the visible noise and the smallest objects were not visible in the noise.

On the CIRS phantom, increasing the emphasis (RE) increased the visibility of small masses (Chart 7A), but did not affect the detection of calcifications or fibers (Chart 7B)



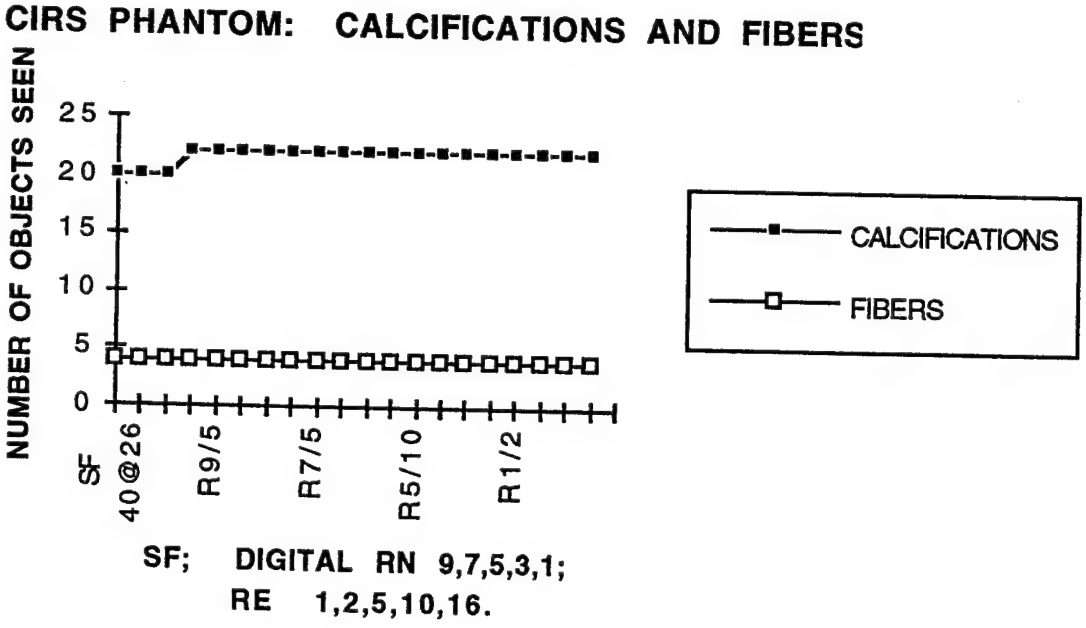


Chart 7: On the CIRS phantom, the detection of masses increases with increased spatial frequency filtering emphasis. The detection of calcifications and fibers did not changes. A. Masses. B. Calcifications and fibers.

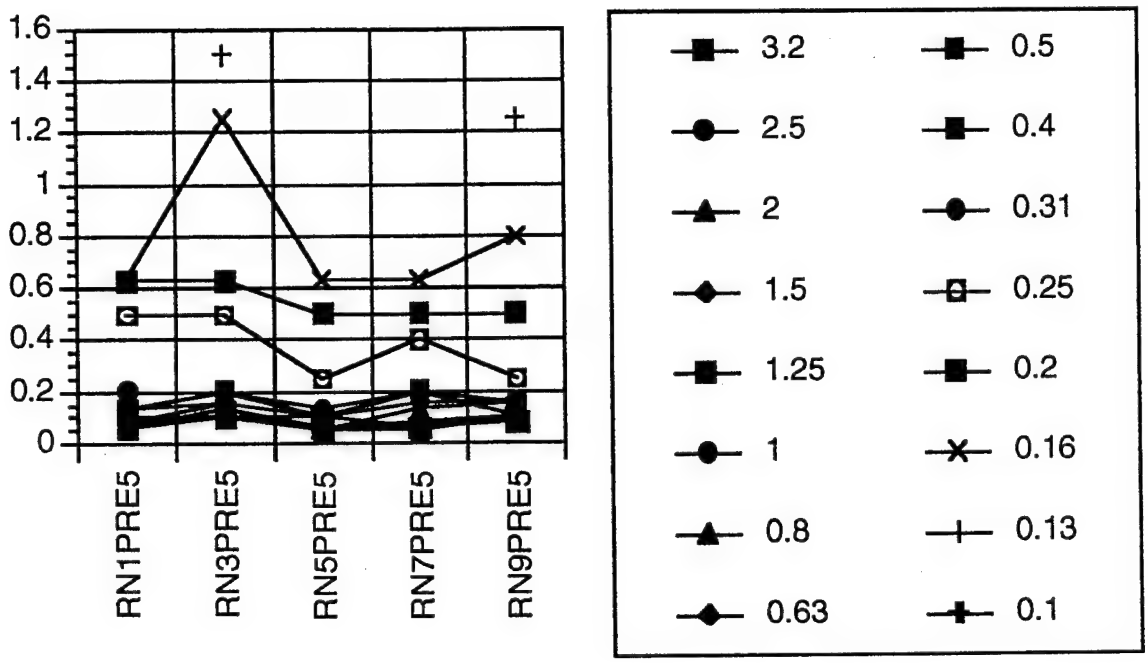


Chart 8: Effect on detectability of small objects with changes in kernel size (CDMAM, using different kernel sizes). There is some improvement in the detection of small objets (0.13 mm in diameter) with kernel size RN(compared to RN 1,3,5, and 7. There is no effect on larger objects.

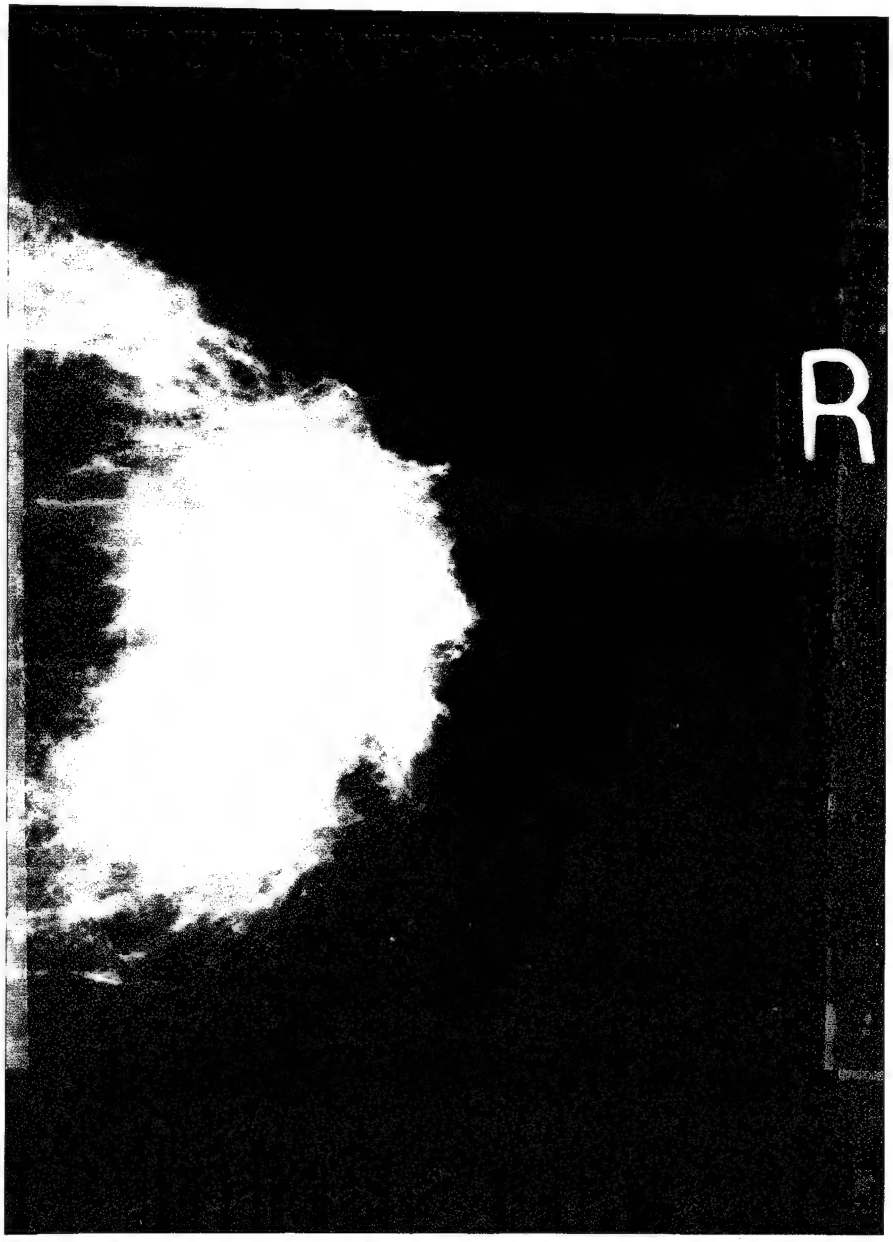
SUMMARY

Image processing of digital breast images can have a marked effect on the appearance of the resulting image and the detectability of objects in it. Tests such as those described above will be used to test potential algorithms for appropriate final image diagnostic quality.

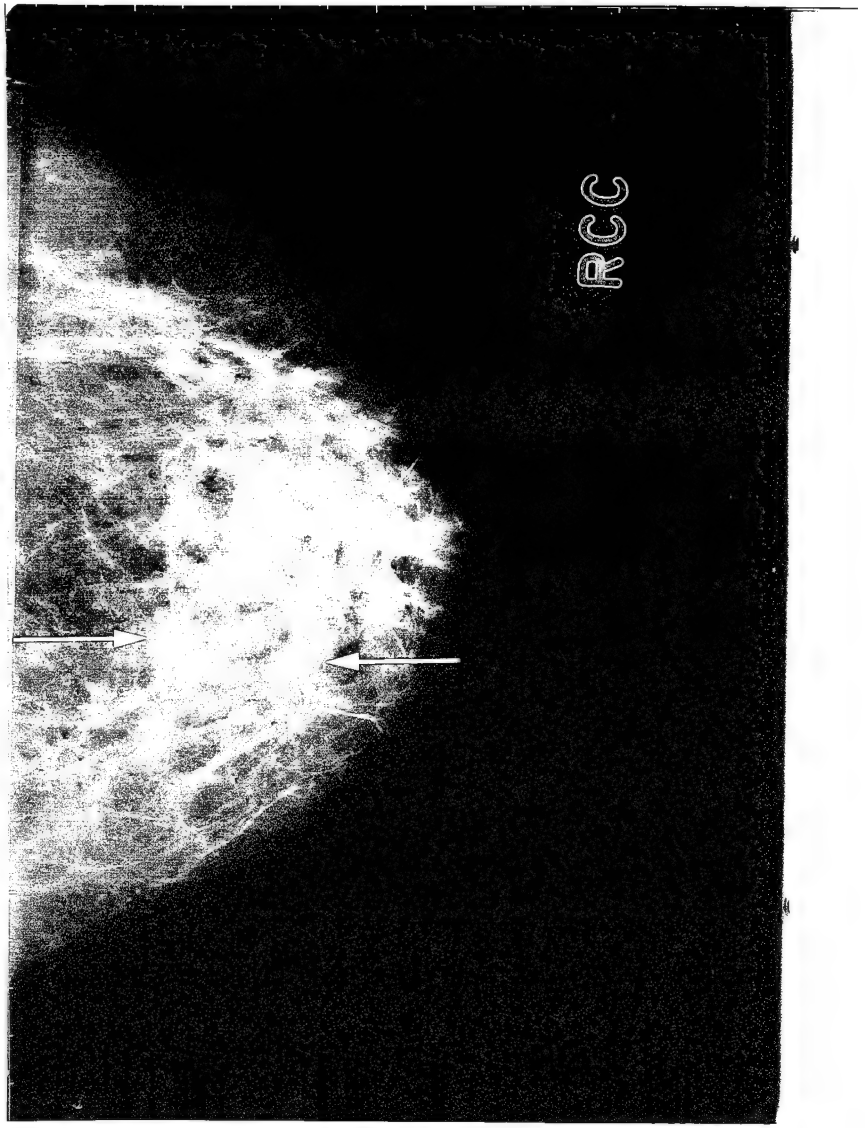
ACKNOWLEDGEMENT:

This research was supported in part by U.S. Army Medical Research Grant DAMD 17-93-J-3008. The content of this report does not necessarily reflect the position or policy of the U.S.Government and no official endorsement should be inferred.

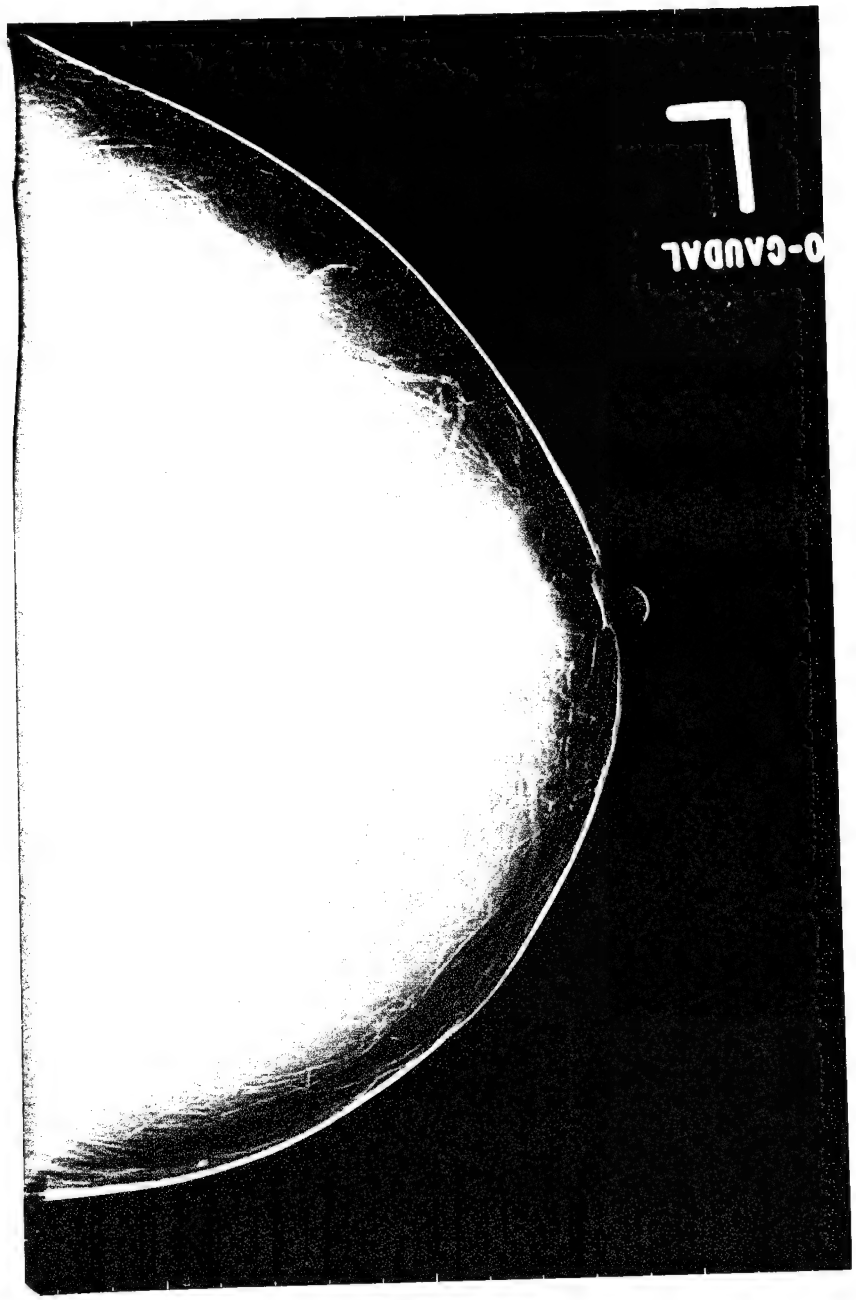
Case 1. Three films. Example of multifocal breast cancer in radiodense breast.
A. Screen film mammogram.



B. Low resolution histogram equalization image. Note visibility of microcalcifications (Arrows)



Case 2: Low resolution histogram equalization
Note skin line visibility and architectural distortion (arrow)



Digital mammography: Tradeoffs between 50 and 100 micron pixel size

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ABSTRACT

Improvements in mammography equipment related to a decrease in pixel size of digital mammography detectors raise questions of the possible effects of these new detectors. Mathematical modeling suggested that the benefits of moving from 100 to 50 micron detectors were slight and might not justify the cost of these new units. Experiments comparing screen film mammography, a storage phosphor 100 micron digital detector, a 50 micron digital breast spot device, 100 micron film digitization and 50 micron film digitization suggests that object conspicuity should be better for digital compared to conventional systems, but that there seemed to be minimal advantage to going from 100 to 50 microns. The 50 micron pixel system appears to provide a slight advantage in object contrast and perhaps in shape definition, but did not allow smaller objects to be detected.

INTRODUCTION

Several sites are working to develop 50 micron digital systems for whole breast digital mammography. There currently exists a 100 micron pixel storage phosphor whole breast digital mammography system. 50 micron digital spot devices also exist that are used for limited views of the breast. 50 and 100 micron film digitization devices are available. Moving from a 100 micron system to a 50 micron system involves costs and benefits. This paper will explore the tradeoffs involved and attempt to model the potential benefits that such a system might have. The potential costs, benefits, and examples of what can currently be seen with 100 and 50 micron pixel systems will be presented.

THE COSTS

The costs of using a 50 micron instead of a 100 micron system include the costs of increased Radiation, Data Volume which will affect the costs of Data processing, Transmission, Storage and Display. Design and manufacturing costs for the new equipment are also important cost considerations.

Increase Radiation

The change from 100 to 50 micron pixels results in four times as many pixels to include the entire breast. X-ray images can be considered to be quantum limited (i.e. everything that can be done to work at minimal patient absorbed dose has been done). If one has two detectors with the same detector quantum efficiency and covering the same area of the breast, the one with four times as many pixels will need four times as much exposure to maintain the same signal to noise ratio and presumably 4 times the patient absorbed dose. Several strategies can be used to decrease the patient dose: One can use a detector with higher quantum efficiency, one can modify or remove the grid from the system (our mammography grid requires us to use 2.2 to 2.5 times the exposure depending on the KVP), one can use a higher KVP (which results in a lower patient absorbed dose at the cost of lower contrast).

Data Volume

If one has four times the number of pixels, one has four times the data volume increasing the costs of data processing, storage and transmission. This increased data must also be displayed. Soft copy displays suitable in luminance for clinical radiology are currently limited to 2 x 2.5 K. Commercially available laser cameras for printing the images have a minimal spot size of 80 microns although 50 micron systems are under development. With an 80 micron laser camera, the breast will be displayed enlarged.

Design and Manufacturing Costs

The development of new devices results in major costs. These must be offset by benefits that most likely have to include the detection of breast cancer at an earlier stage with, therefore, an improved prognosis.

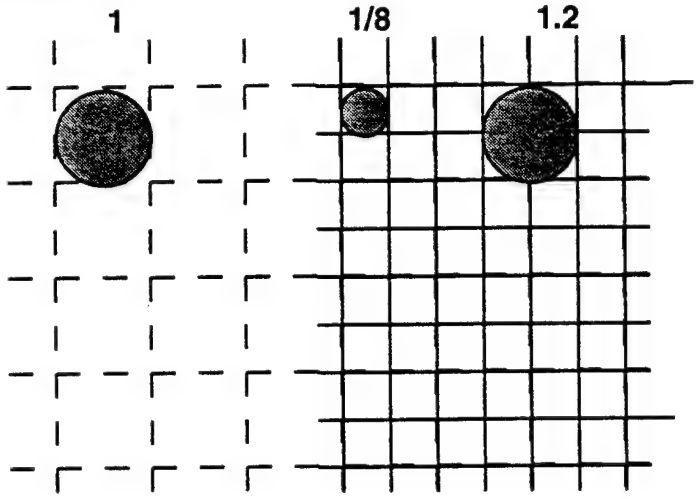
BENEFITS

There are three potential benefits that could occur in digital mammography from the use of a smaller pixel size: the detection of smaller objects, better definition of the shape of objects and a more accurate count of the number of objects present.

Detection of smaller objects:

The detection of smaller objects within the breast should allow the identification of smaller breast cancers. A 50 micron system might show smaller objects than a 100 micron system. Detection of objects depends on their ability to absorb x-ray photons. As objects become smaller they will usually also become thinner. If one has a 100 micron object and a 50 micron object, the absorption of the 50 micron object will be 1/8 that of the 100 micron object. In order to detect a 50 micron object, one would need to be able to use a high contrast look up table and have a relatively noise free background. The use of smaller pixels is likely to increase the noise level. It is therefore unlikely that a 50 micron system will be able to detect smaller objects than a 100 micron system given similar image processing capabilities.

V=4/3Pi r^3



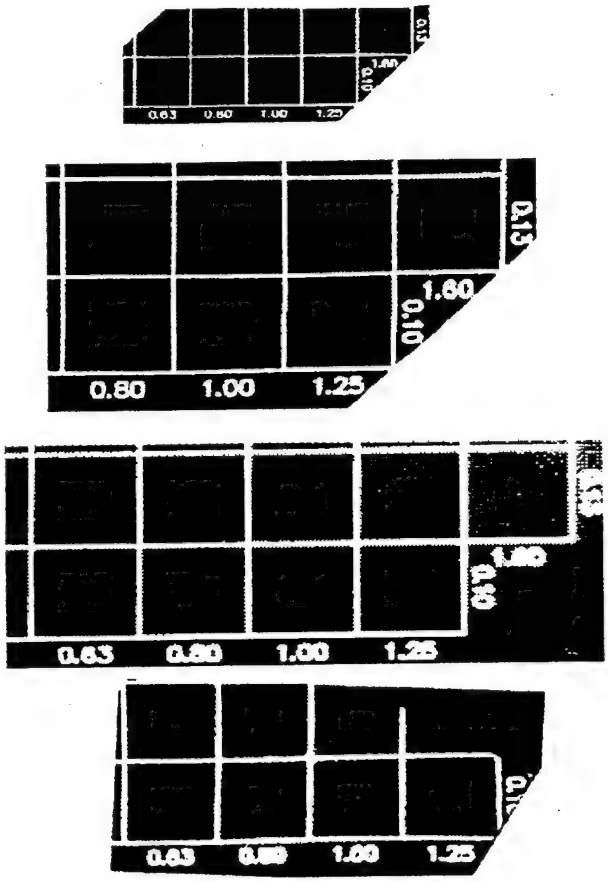
In our experiments, both the 100 and 50 micron systems allowed us to see objects of the same size.

TABLE OF SMALLEST OBJECT SEEN

Test Object	Screen Film	100 micron phosphor	50 micron CCD
CDMAM	130. 100 at 5x mag	100 at 1 micron thick	100 at 0.8 microns thick
CIRS Detail	240	160	160
RMI 156	240 (3/6)	240 (3/6))	240 (3/6)
Steel Fleck	100	50 (noisy, high contrast)	100
CIRS Half Round	160	160	160

Contrast

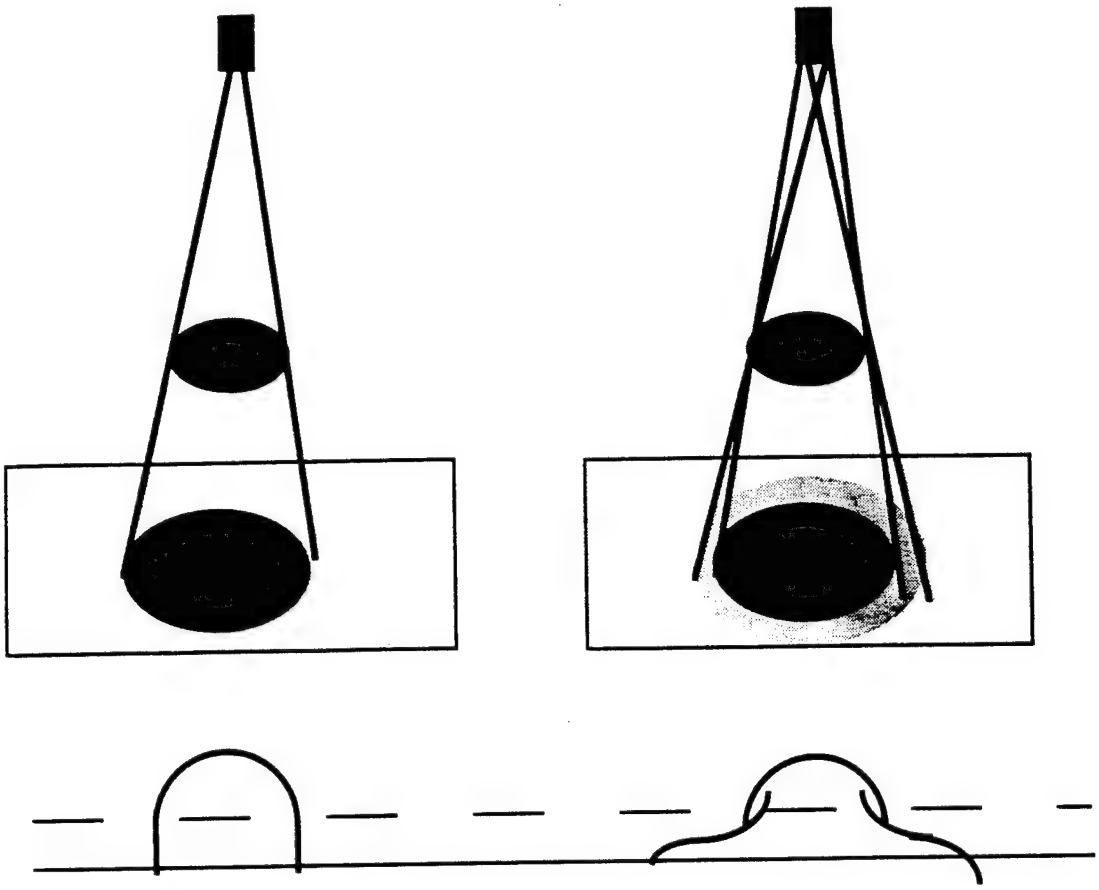
The contrast of the objects with the 50 micron system was slightly higher as demonstrated in the pictures of the CDMAM phantom shown below.



Nuclear Associates CDMAM Phantom: Screen film digitized at 100 microns and 50 micron pixel, 100 micron storage phosphor image, 50 micron digital spot device. The screen film image can show the 130 micron objects. The 100 micron system shows 100 micron objects at the 1.25 and 1.00 micron thicknesses. The 50 micron digital spot device shows the 100 micron object at 0.80 microns of thickness.

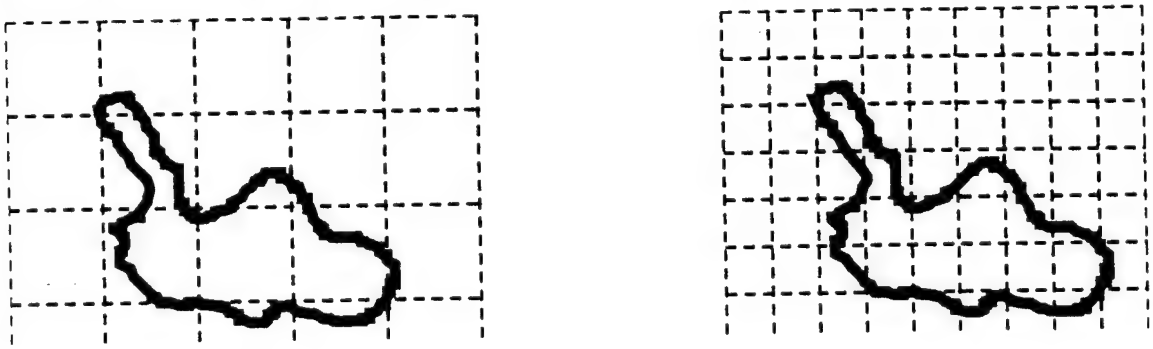
Penumbra

The penumbra around an object caused by the finite size of the focal spot results in a projection of the object that is less distinct at its edges than the true object (i.e. it has a lower contrast definition at its edges. Small faint objects would tend to be less distinct than larger or higher contrast objects. If one is using a 300 micron focal spot, a 65 cm focal spot detector distance and a 3 cm object detector distance, the penumbra is approximately 15 microns on each size.



Better definition of object shape

Object shape evaluation depends on the number of pixels that an object is superimposed on. A 50 micron system could result in improved visualization of shape. Many writers have commented that shape is an important criteria in determining the potential for malignancy in microcalcification. Since screen film system can detect in the intact breast objects with a minimum object size of 250-300 microns, one would have to demonstrate that the difference in shape definition between an object projected on 9 pixels and 36 pixels is clinically important. The penumbra resulting from the measurable size of the focal spot will decrease the sharpness of the image and therefore the ability to determine shape.



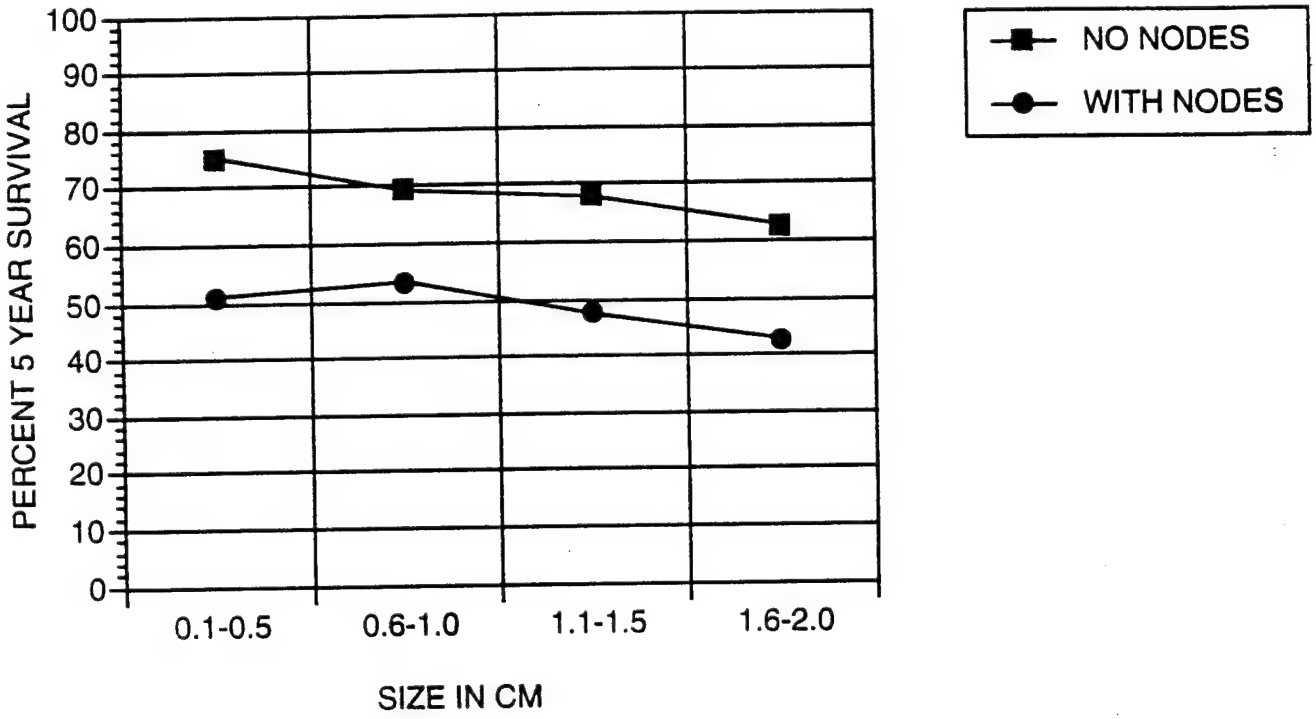
THE GOAL OF DIGITAL MAMMOGRAPHY: FINDING SMALLER BREAST CANCERS

The goals of digital mammography are (1) to allow the detection of smaller breast cancers and (2) to improve the differentiation of benign and malignant lesions. One or both of these should occur to justify the expenses in the use of digital mammography. While there may be a few instances where digital storage or transmission might be necessary, in general, that would not result in a sufficient volume of demand for machines to justify their cost of development.

What is the possible benefit and what is the possible risk from detecting smaller objects?

To demonstrate a true benefit from the detection of smaller objects that could be related to cancer, one would have to show that this earlier detection affects the long term outcome patient disease free survival. One can use a surrogate for this by showing that in historic data smaller cancers indeed do have a better prognosis. One can, using the data from Bedwani demonstrate that detecting cancer when it is 0.5 cm or less in size does afford a better prognosis than detecting it 0.6-1.0 cm in size.

FIVE YEAR SURVIVAL AFTER REMOVAL SMALL INVASIVE BREAST CANCERS WITH NO EVIDENCE OF DISEASE

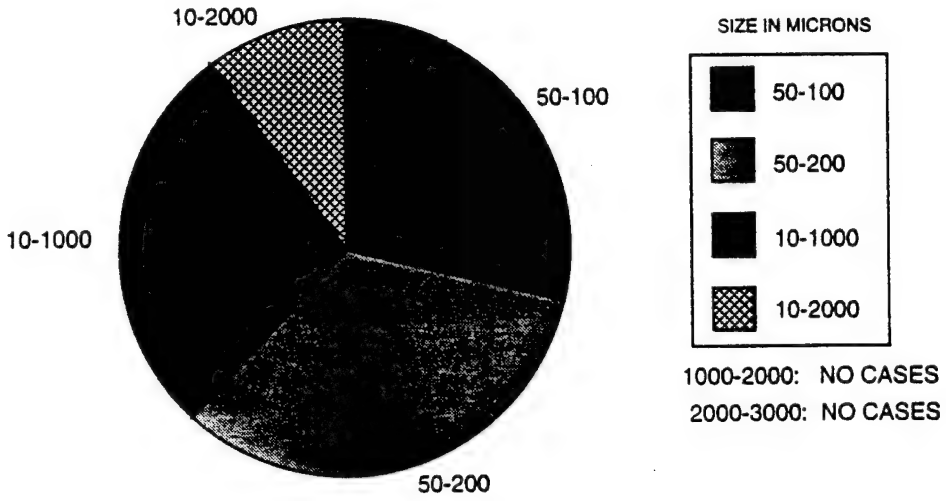


Bedwani et al. Cancer 47:2769-2778, 1981

Cancer with calcifications to small to be seen with conventional mammography

Cancer can containcalcifications too small to see with conventional screen film mammography. Egan found that in specimen radiographs that microcalcifications in 28 percent of patients were limited to those between 50 - 100 microns in size. This is usually considered too small a size to be seen by conventional screen film mammography.

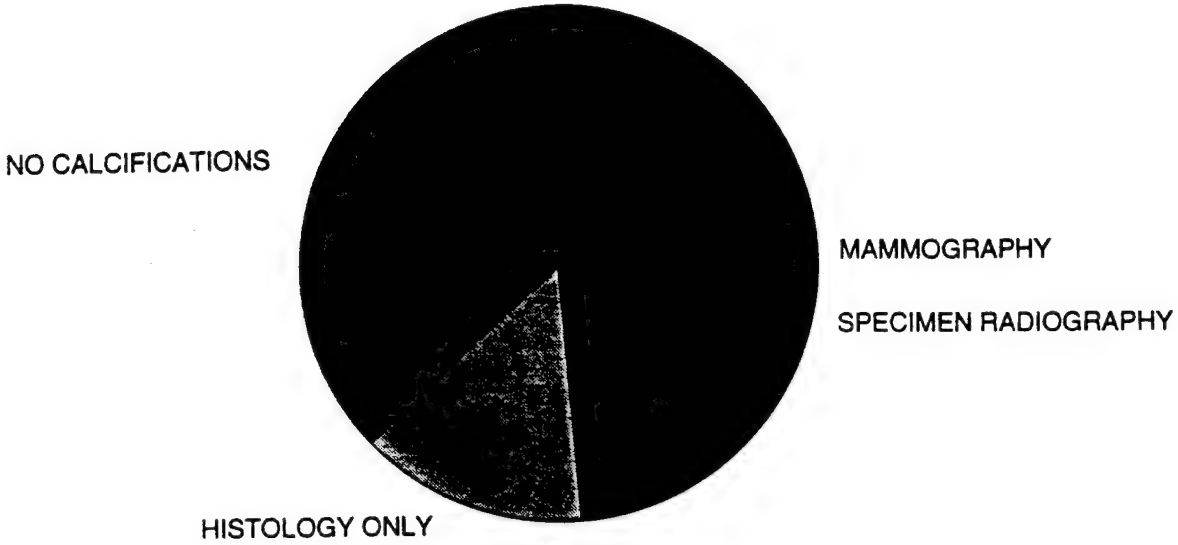
SIZES IN MICRONS OF MICROCALCIFICATIONS IN 115 BREAST CANCERS
WITH MICROCALCIFICATIONS AS ONLY SIGN OF CANCER



RL Egan. Radiology 137:1-7, 1980

The work of Millis also supports this conclusion.

RADIOLOGY PATHOLOGY CORRELATIONS
OF MICROCALCIFICATIONS IN BREAST CANCER

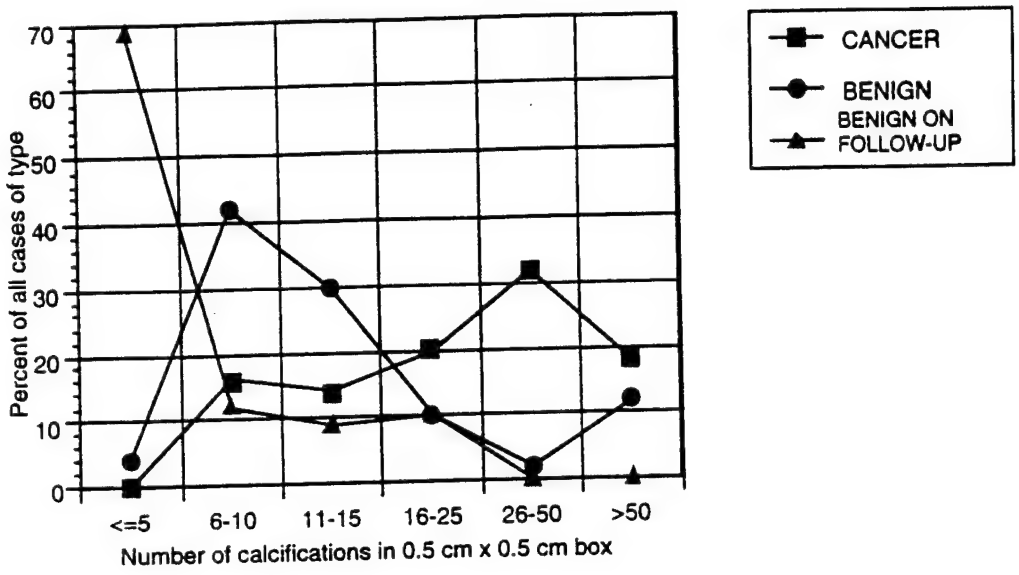


MILLIS, BRITISH J OF RADIOLOGY. 1976. 49:12-26

Number of microcalcifications

Improved resolution should allow an improved count of the number of microcalcifications present. This number appears to correlate with the likely presence of cancer.

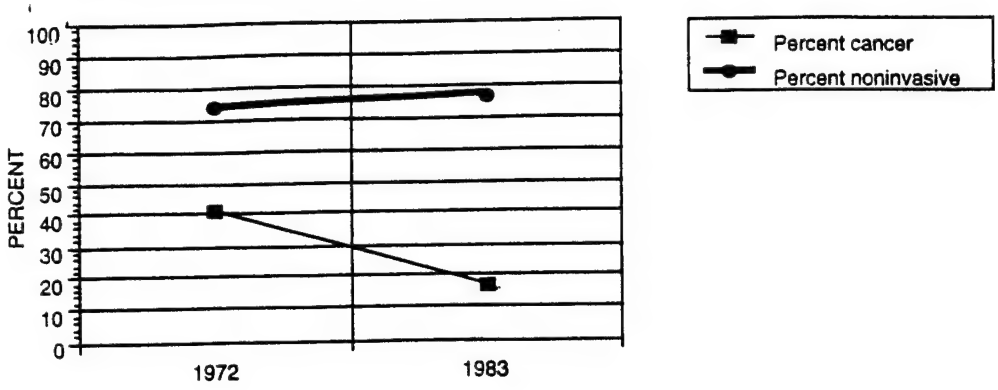
NUMBER OF MICROCALCIFICATIONS IN BENIGN AND MALIGNANT CASES



Egan, Radiology 137:1-7, 1980

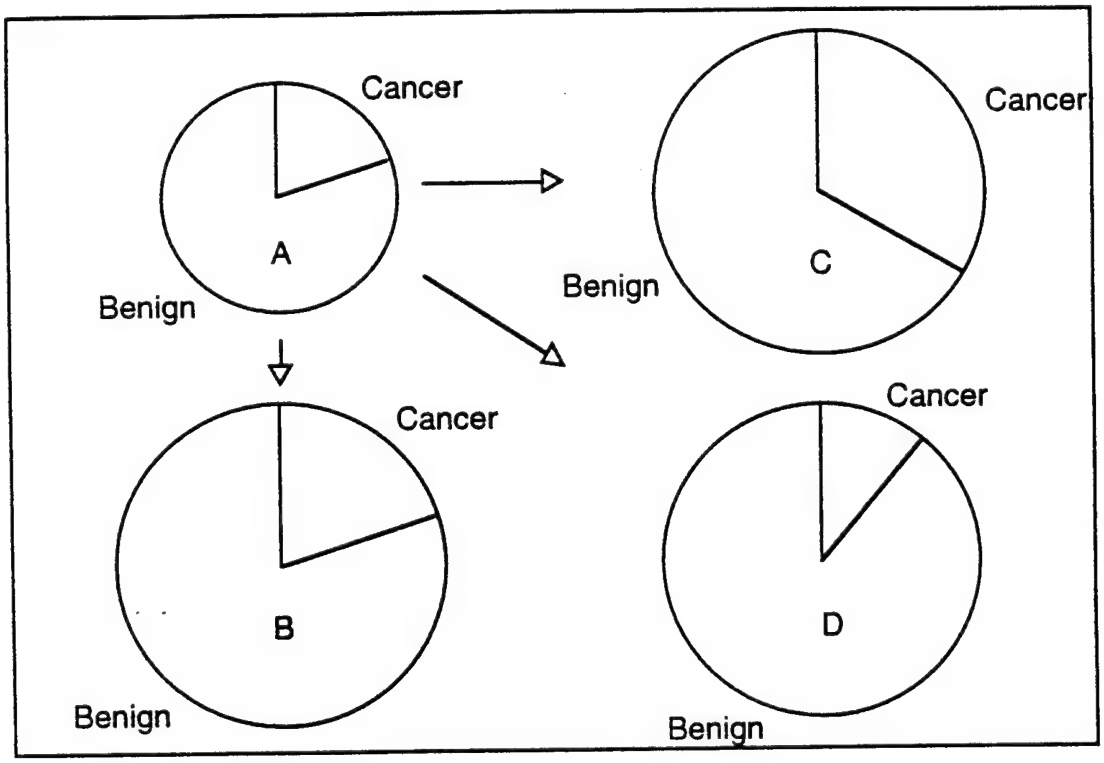
The risk of detecting smaller signs of possible cancer is related to the concern that finding smaller objects might change the ratio between malignant and benign biopsies. Currently, we do approximately three biopsies for each cancer detected. In other centers it can be 1 in 5. In one series, only 17 % of biopsies done for microcalcifications showed cancer. If one finds smaller microcalcifications and smaller masses, one might find that the frequency of biopsies demonstrating cancer had increased or decreased. I am aware of no data on this issue. The data of Powell shows that from 1972 to 1983, the number ratio of cancers to benign disease detected decreased in patients biopsied for microcalcifications. A recent unpublished series (Smith) shows a 17 percent ratio of cancer in stereotactic biopsy, the same as in Powell's series from 1983.

BIOPSIES FOR MICROCALCIFICATIONS AS ONLY ABNORMALITY ON MAMMOGRAM



Powell et al. Annals of Surgery 197: 555-559, 1983

As shown in this drawing, there are several potential outcomes should new technology allow the detection of smaller lesions.

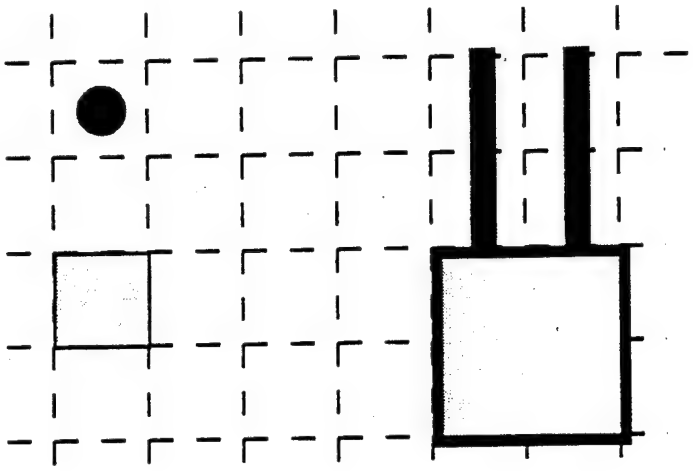


In this drawing, let A represent the current detection of microcalcifications and small masses. If we increase the detection rate as shown in B, then the percentage cancers remain the same and we have not altered the expected cost of detecting cancer. Ideally, as shown in C, we would hope that the better definition of detail would allow us to improve the proportion of cancers detected. But, as shown in D, the proportion of cancers might decrease resulting in an increased number of breast biopsies with little or no improvement in the detection of breast cancer. Which of these scenarios will occur is unknown.

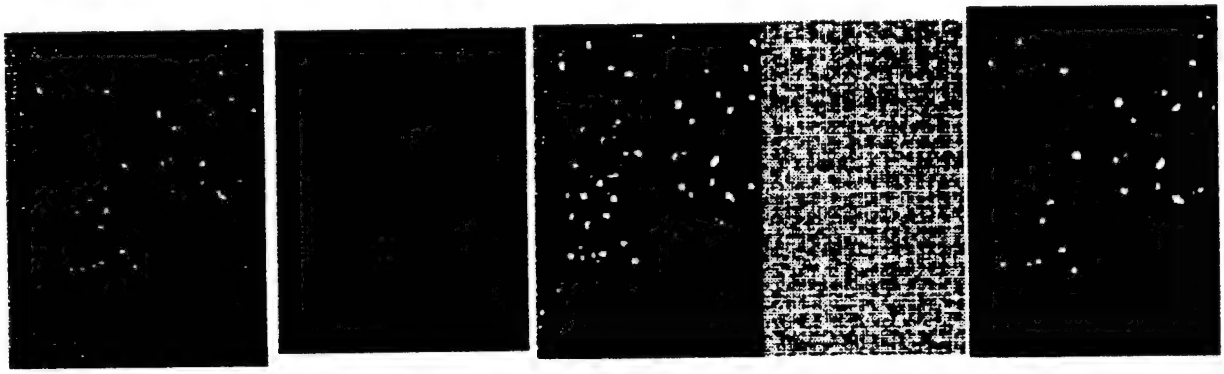
OBJECT VISIBILITY: WHAT CAN BE SEEN

Detection vs. Resolution

Detection and resolution are different. One can detect an object smaller than the pixel size if it is of sufficient contrast because its effect on the pixel will be averaged over the pixel.



Detection is related to object contrast, pixel size and background noise. A high contrast object can be seen even if it is smaller than the pixel as shown in this home made test object. 50 micron steel flecks can be seen with a 100 micron pixel (in a visibly noisy background), but cannot be detected with the 50 micron digital spot device.



Homemade test object with steel flecks 50 microns and larger. A. Direct film exposure. On the original 50 micron objects can be seen and measured with magnifier. B. Screen film mammogram. 50 micron flecks seen with difficulty. C. Storage phosphor 100 micron pixel system 50 micron flecks (arrows) can be easily seen. D. Subtraction image done with two different exposures and storage phosphor imaging plates documents that 50 micron objects are not noise. E. 50 micron CCD image. With the image processing used, the 50 micron flecks cannot be seen.

BIBLIOGRAPHY

Bedwani R, Vana J, Rosner D, et al. Management and survival of female patients with "minimal" breast cancer. Cancer 47:2769-2778, 1981

Egan RL, McSweeeney MB, Sewell CW. Intramammary calcifications without an associated mass in benign and malignant diseases. Radiology, 1980. 137:1-7.

Millis rm, Davis R, Stacey AJ. The detection and significance of calcifications int he breast: a radiological and pathological study. British J of Radiology, 1976. 49:12-26

Powell RW, McSweeney MB, Wilson CE. X-ray calcifications as the only basis for breast biopsy. Annals Surgery 1983. 197:555-559.

Smith D. Personal communication regarding stereotactic biopsy results. August, 1994.

Freedman M, Pe E, Nelson M, Lo S-C B, Mun S K: Digital Mammography: Demonstration of a Method of Achieving Adequate Resolution on a Storage Phosphor System. CAR 93, 7th International Symposium, Berlin, Germany (June 24-26, 1993); 783pp.

Freedman M, Pe E, Zuurbier R, Katial R, Jafroudi H, Nelson M, Lo S-C B, Mun S K: Image Processing in Digital Mammography. SPIE: Medical Imaging, Vol. 2164 (1994); 537-554pp.

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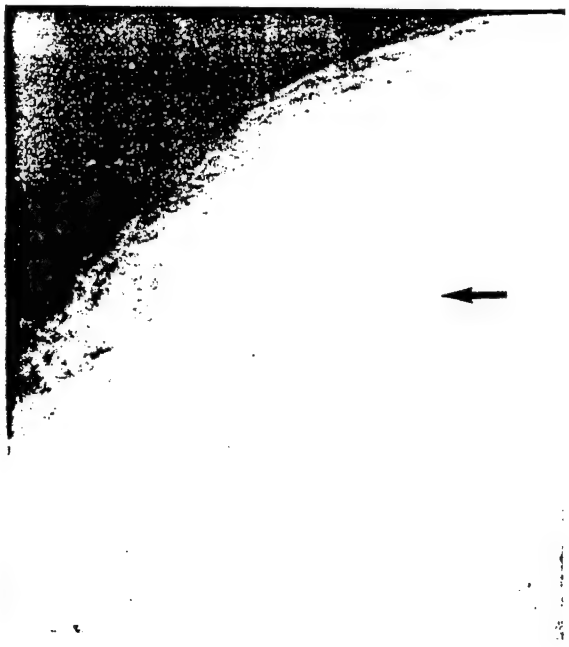
Case 1. There are various methods of image processing available for enhancing the visibility of findings in t breast in digital mammography. The following demonstrate processing for emphasizing small details (microcalcifica in a complex pattern breast.

ORIGINAL SCREEN/FILM Image 1



DIGITAL AT SAME EXPOSURE Image 2

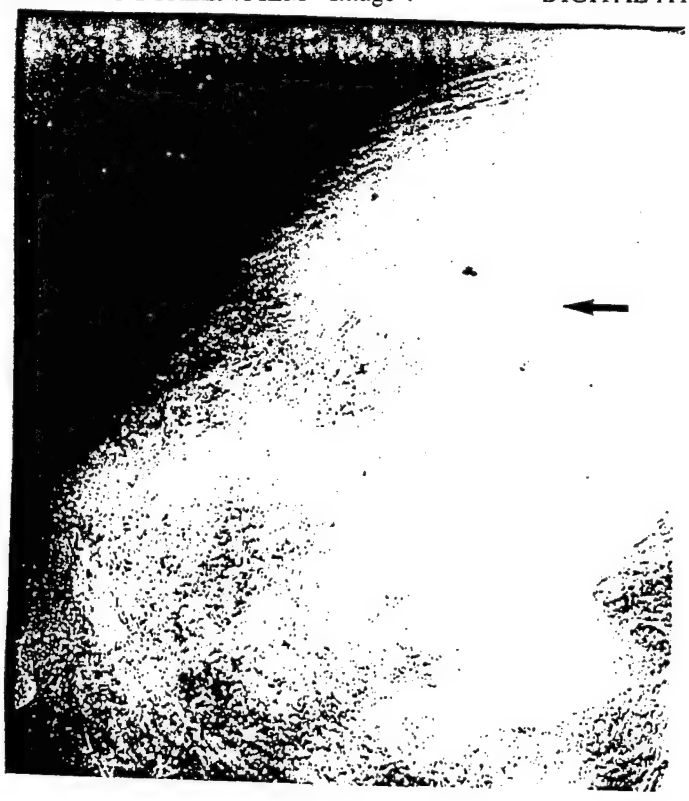
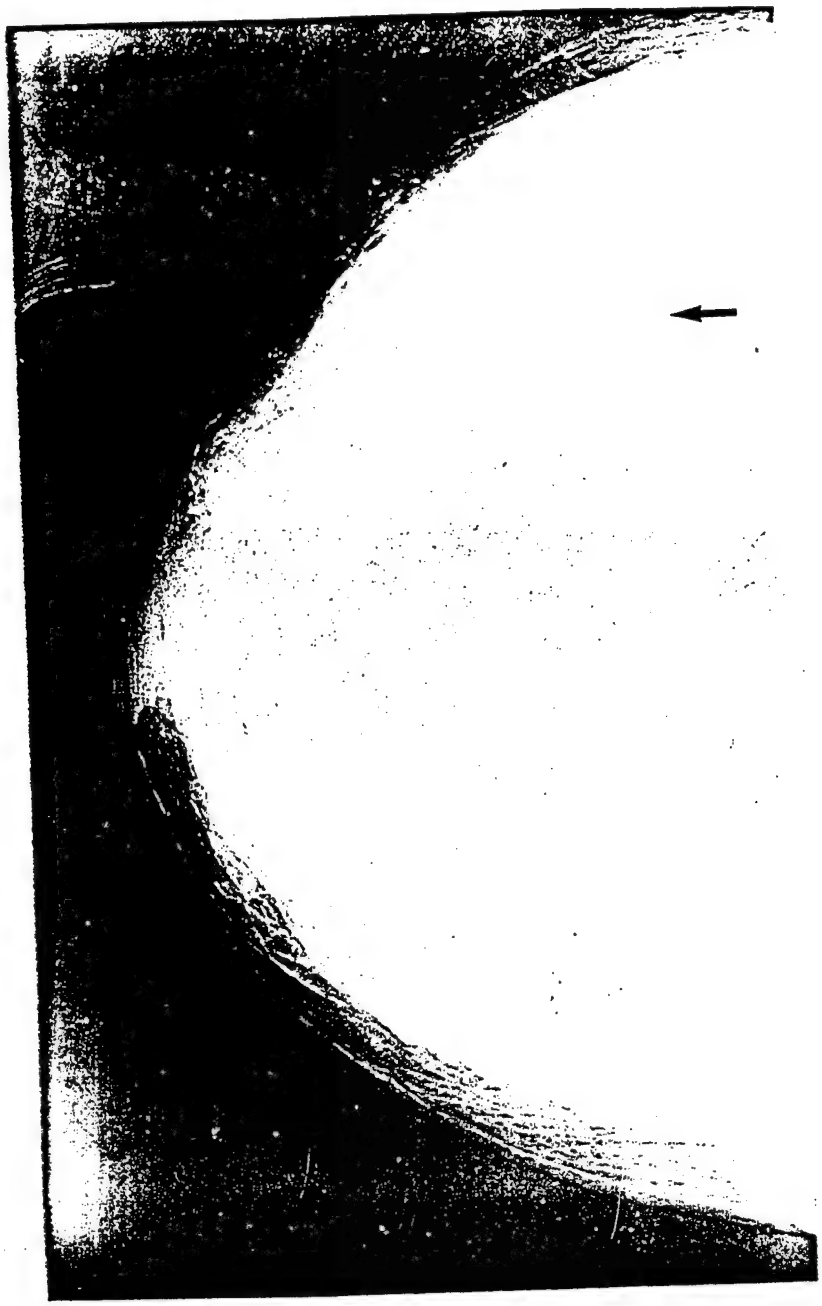


IMAGE PROCESSING FOR DETAIL *Image 3* The microcalcifications are enhanced, but the complex pattern is also enhanced. Noise is also enhanced.



ADDITIONAL PROCESSING TO SIMPLIFY THE COMPLEX PATTERN OF THE BREAST IMPROVING THE CONSPICUITY OF MICROCALCIFICATIONS. *Image 4* The microcalcifications have increased conspicuity because the background pattern of the breast has been suppressed.

CASE 2

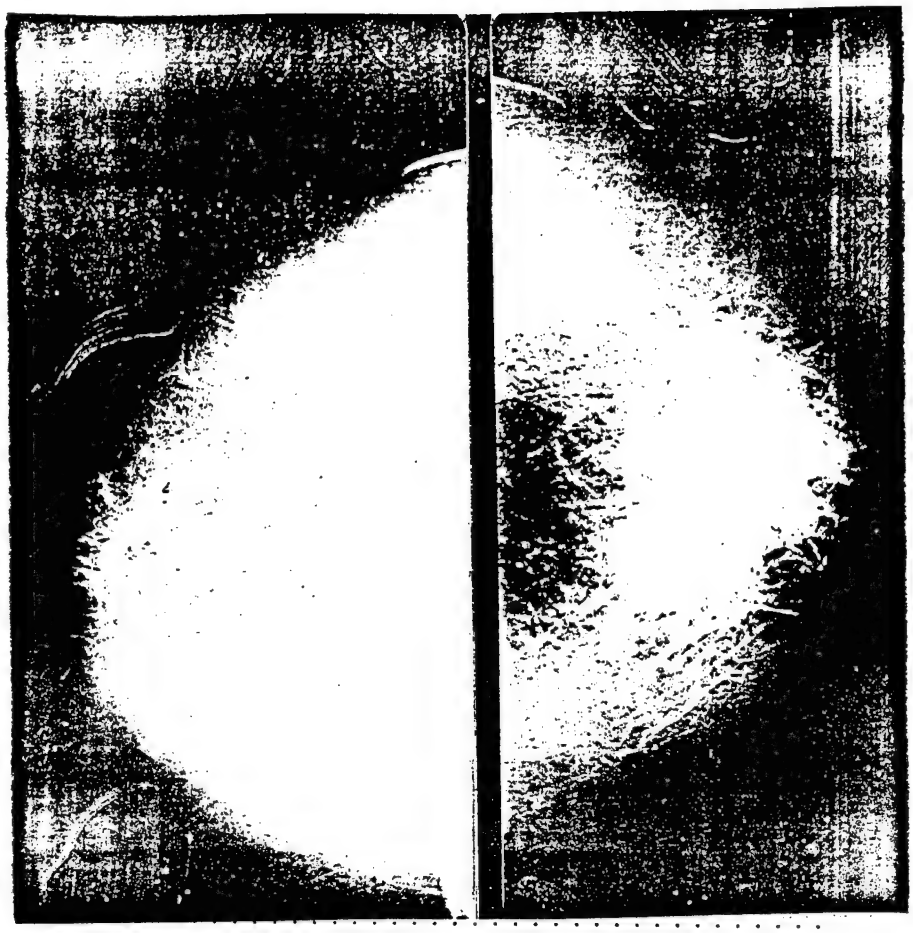
This case demonstrates the functionality of image processing to change the optical density of large regions of increased radiodensity, improving the visibility of microcalcifications.

FINDINGS: Asymmetric density with microcalcifications

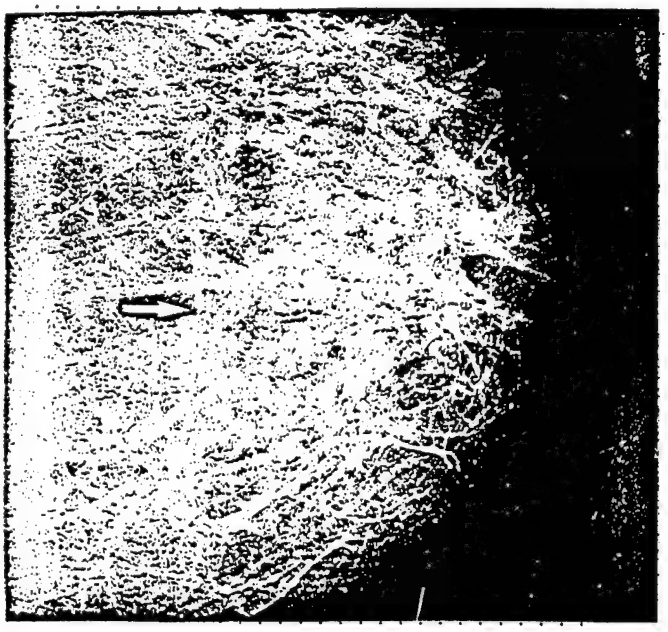
PATHOLOGY: 3 cm ductal carcinoma with microinvasion

IMAGE PROCESSING: Frequency enhancement for microcalcifications and optical density shift specific to the tissue density

A. Conventional original RCC film *Image 5*



B. Digital at same exposure of LCC and RCC twin-format image *Image 6*



C. Processed digital image: *Image 7*. Low spatial frequency equalization of optical densities

On this image, the groups of microcalcifications (arrow) are easier to see than on either the screen film or film look alike digital images. The image processing has allowed us to look through the asymmetric breast density and see the microcalcifications within it.

CASE 3
FINDINGS: Microcalcifications within focal tissue density
PATHOLOGY: Fibrocystic changes with calcifications and ductal hyperplasia
IMAGE PROCESSING: High frequency enhancement with high and low spatial frequency equalization

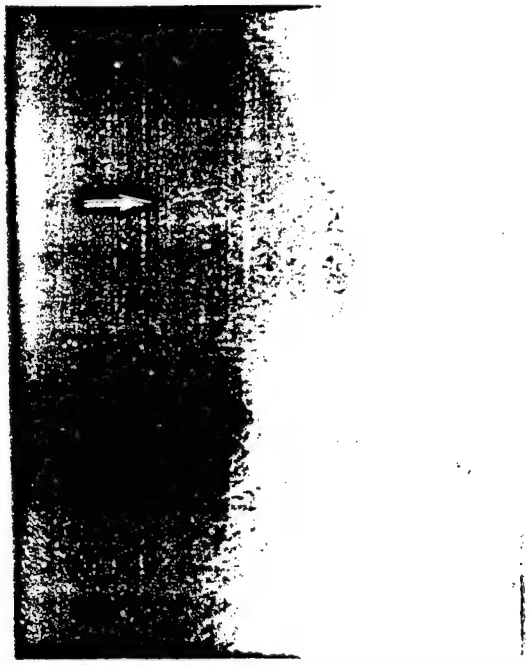
A. Conventional original film *Image 8*

B. Digital at same exposure *Image 9*

C. Processed digital image: *Image 10*
High frequency enhancement with low optical density equalization

D. Processed digital image: *Image 11* High frequency enhancement with high and low optical density equalization. The visualization of the skin line is improved. One can still see the microcalcifications and mass. The architectural distortion is clearer.

CASE 4
FINDINGS: Mass upper outer quadrant left breast
PATHOLOGY: Benign recurrent fasciitis



A. Conventional original film *Image 12.* The focal region of abnormal tissue close to the skin line is almost hidden.

B. Digital at same exposure *Image 13*

C. Processed digital image: *Image 14*
Low frequency enhancement with high optical density equalization. The focal tissue density lying close to the skin, high in the breast is much easier to identify., but the overall tissue appearance is distorted.

D. Processed digital image: *Image 15*
High frequency enhancement with high and low optical density equalization. The skin line is easily seen as is the tissue area of interest. The microcalcification is seen with slightly less contrast than on the other images.

Digital Mammography in the Radiodense and Complex Pattern Breast

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Abstract

The sensitivity of mammography for the detection of breast cancer is decreased in the radiodense breast. Storage phosphor digital radiographic systems have a wider latitude of exposure than conventional mammographic screen film systems. By using low resolution histogram equalization one can produce a mammographic image of the breast that retains the high frequency information that defines the edges of microcalcifications, architectural distortion and some masses but which, at the same time, allows one to look through into regions of increased breast radiodensity and identify microcalcifications within them. This paper demonstrates the effect of this special form of image processing.

Key Words: Breast Cancer Digital Mammography radiodense young women histogram equalization image processing.

Introduction

Conventional screen film mammography has a high sensitivity (88%) for the detection of breast cancer. In younger women, the sensitivity is substantially below that (60-68%) (Tabar). If one looks at reports summarizing the image characteristics of cancers missed on screening mammography, many of them occur in regions of increased breast radiodensity (Farria, Bird, Harvey, Silverstein). Our previous reports to SPIE Medical Imaging (Freedman, 1994 and 1995) reported that digital mammography had a wider range of effective exposures than did screen film mammography, as summarized in the following chart:

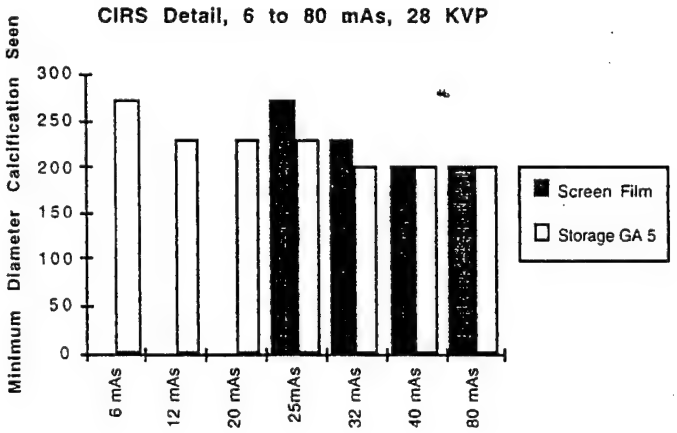
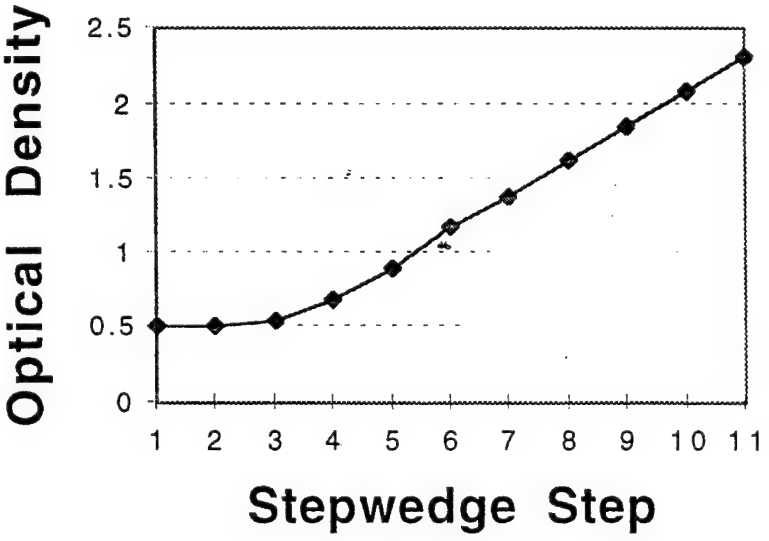


Chart 1: This chart demonstrates the smallest sized test details visible on the CIRS Detail Phantom as exposure is varied, comparing two systems: conventional screen film mammography and Fuji Digital Storage Phosphor radiography, processed in Sensitivity Mode. At low exposure levels, the digital system allows the detection of simulated microcalcifications that cannot be seen in the conventional system. This is analogous to detecting microcalcifications in radiodense regions of the breast. (From Freedman, 1995)

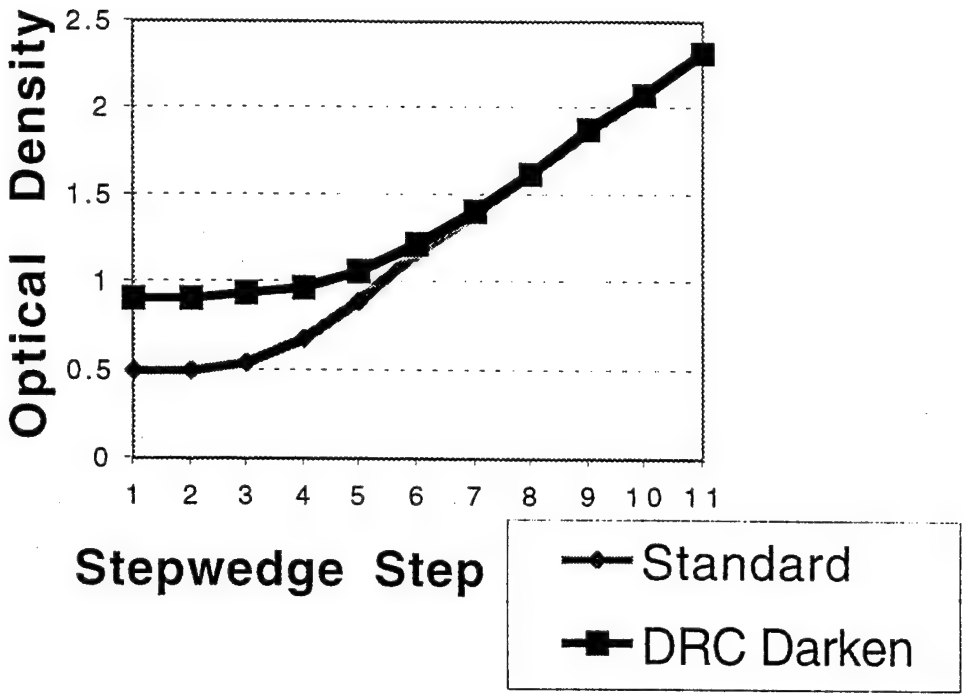
If one attempts to demonstrate this broad range of exposures, however, one ends up with an overall low contrast image--similar to the effect that would occur if one used a low contrast screen film system for mammography. The method for displaying this range of information without compromising local contrast of microcalcifications, breast fibers and masses is the subject of this report.

At SPIE Medical Imaging 95, we reported on the use of Dynamic Range Control (DRC) in images of the feet and wrists (Legendre). This report showed that if one used this process that one could have dramatic impact on the regional optical density of an image while preserving the contrast in fine detailed structures. The formulas for DRC processing were discussed at that time. It is easiest to think of the process we will be describing as the creation of a low resolution mask to which we apply histogram equalization which is then combined with the original image. The result is an image in which high frequency data is preserved, but regional gray scale information is compressed. The effect in mammograms, as will be shown, is to preserve the visibility of microcalcifications, breast fibers and the edges of well defined masses, while bringing the total image into a grayscale range so that one can display, potentially, from the skin line to the depths of the densest part of the breast in one image. DRC allows one to decrease high pixel value regions, increase low pixel value regions, or simultaneously compress the low and high pixel value regions. Because it is active only at low spatial frequencies, it preserves most of the structural information of high frequency structures such as microcalcifications. By appropriately adjusting the kernel size used in this process, one can, as shown below in Case One, "simplify" the complex pattern of many small focal radiodensities seen in some women with radiodense breasts.

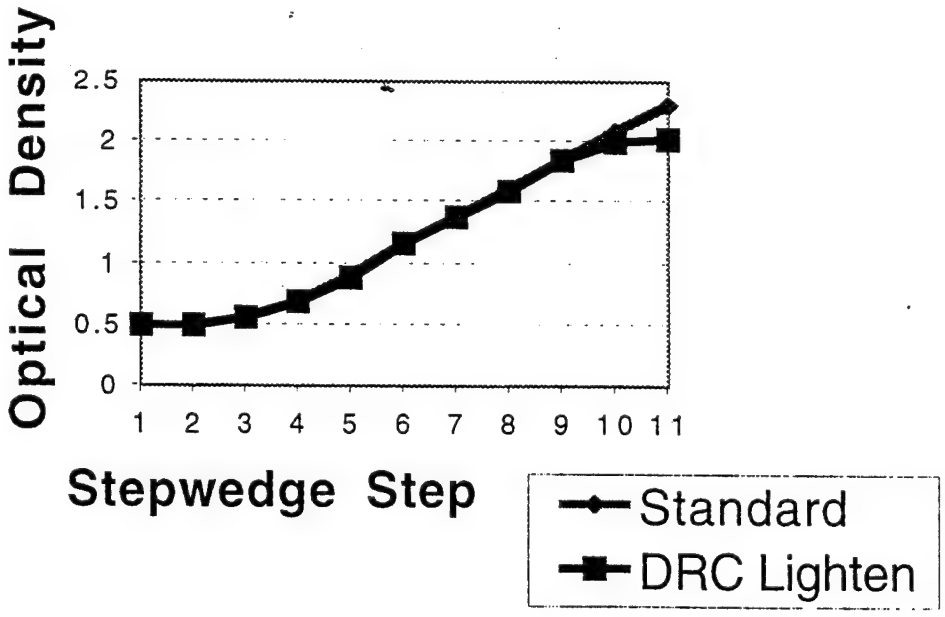
Chart 2. These charts demonstrates the effects of DRC.



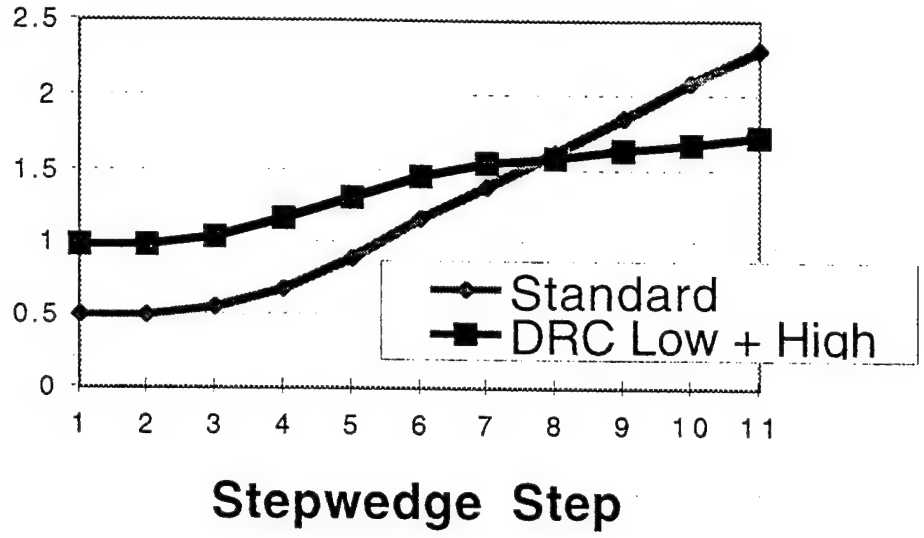
2A: The standard look up table. This is the approximate look up table for the high frequency components of the image.



2B: DRC effect of increasing the low optical density regions of the image.



2C: DRC effect of decreasing the high optical density regions of the image.



2D: DRC effect of decreasing the high optical density regions and increasing the low optical density regions of the image.

Methods: Digital mammograms are obtained with the standard exposure used for screen film mammography in women coming for breast biopsy using HR-V imaging plates and a Fuji 9000 Computed Radiography Plate Reader. Image processing includes the use of Fuji Dynamic Range Control with special equalization curves requested and designed by us. Each image is individually manually optimized for its complexity of pattern. More than 130 digital mammogram/screen film mammogram/specimen radiograph sets including more than 30 cancers have been assembled. ROC reading is pending.

Discussion

Low resolution histogram equalization appears to provide improved conspicuity of abnormalities within the radiodense breast by balancing the wide range of object radiodensities within the breast. This image processing approach can be reached by several methods and we are currently working to optimize a system based on wavelet decomposition as well. Digital acquisition appears optimal for this system since it can allow the recording of a wider range of exposure information than conventional screen film mammography. It is possible that this processing could also prove effective if a wide latitude film were used for mammographic image capture for secondary digitization, but this effect does not occur with standard screen film images with secondary digitization.

Inspection of these images should reveal problems occurring from noise in regions of increased breast radiodensity processed with this algorithm. On conventional mammograms, these regions would be clear or nearly clear. Because of the noise secondary to under-exposure, these "recaptured" regions have decreased conspicuity of the smallest calcifications compared to fully exposed regions of the imaging plate as reflected in the Chart 1 printed above.

Summary

Low resolution histogram equalization appears to offer advantages in the display of mammograms in the radiodense and complex pattern breast. The range of tissue densities that can be evaluated on these new images is greater than those normally visualized in the radiodense breast. The system still requires individual optimization of image appearance, but we expect that patterns will emerge that will eventually allow several standard forms of this image processing to be applied routinely. We are about to start our ROC reading to determine whether this new method of image processing does indeed enhance the detectability of breast cancer in the radiodense breast.

Bibliography

Bird RE, Wallace TW, Yankaskas BC. Analysis of cancers missed at screening mammography. Radiology 1992; 184:613-617.

Farria DM, Mund DF, Bassett LW. Evaluation of mised cancers using screening mammography. (Abstract) AJR 1995; 164S:126

Freedman M, Pe E, Zuurbier R, Katial R, Jafroudi H, Nelson M, Lo S-C B, Mun S K: Image Processing in Digital Mammography. SPIE: Medical Imaging, Vol. 2164 (1994); 537-554pp.

Freedman MT, Steller D, Jafroudi H, Lo SCB, Zuurbier RA,Katial R, Hayes W, Wu YC, Lin JS, Steinman R, Tohme WG, Mun SK. Digital Mammography: effects of decreased exposure. SPIE Medical Imaging 1995. Paper 2432-49. (1995)

Legendre K, Steller D, Freedman M, Mun S K: Single-image Hardcopy Display of Musculoskeletal Digital Radiographs. SPIE: Medical Imaging (1995). Paper 2436-19.

Harvey JA, Fajardo LL, Innis CA. Previous mammograms in patients with impalpable breast carcinoma: Retrospective vs blinded interpretation. AJR 1993; 161:1167-72.

Silverstein MJ, Gamagami P, Colburn WJ, et al. Nonpalpable breast leasions: Diagnosis with slightly over-penetrated screen-film mammography and hook wire directed biopsy in 1014 cases. Radiology 1989; 171:633-638.

Tabar L, Fagerberg G, Duffy SW et al. Update of the Swedish two-county program of mammographic screening for breast cancer. Radiologic Clinics of North America 1992; 30:187-210.

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Digital Mammography: An evaluation of the Shape of Microcalcifications

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Abstract

Microcalcifications can be identified on mammograms in approximately 50-55 % of breast cancer cases. Three factors affect the ability to use the presence of microcalcifications as a sign of cancer. They must be seen (conspicuity), their shape must be assessed (to differentiate benign and malignancy associated shapes) and they should be countable since the greater the number of clustered calcifications, the more likely they are malignancy associated. Concern has been expressed that digital systems with their inherently worse resolution would not allow adequate shape information to be captured. Using a 100 micron pixel size storage phosphor system we randomly selected 20 cases, 10 benign and 10 showing malignancy on biopsy and asked four radiologists to assess the calcifications present comparing the original screen film and the digital images and using the screen film biopsy specimen radiograph as ground truth. The preferences were mixed with some radiologists preferring screen film and others the digital images. Whatever their preferences, the radiologists were unable to use the shape criteria to distinguish benign and malignant cases in this case sample.

Key words: digital mammography microcalcification shape number conspicuity breast cancer

Introduction

Microcalcifications can be identified on mammograms in approximately 50-55 % of breast cancer cases. Three factors affect the ability to use the presence of microcalcifications as a sign of cancer. They must be seen (conspicuity), their shape must be assessed (to differentiate benign and malignancy associated shapes) and they should be countable since the greater the number of clustered calcifications, the more likely they are malignancy associated.

Certain physical properties of screen film mammography suggest that it should be better in evaluating the shape and number of calcifications: Screen film mammographic systems have higher inherent resolution than both 50 and 100 micron pixel digital systems. Screen film systems have resolution in the range of 17-20 line pairs per mm (lpm). 100 micron pixel systems have a theoretical 5 lpm and 50 micron systems a theoretical 10 lpm. The high resolution of film screen mammography is, however, at low contrast.

Certain physical properties of digital systems suggest that they should be better in providing improved conspicuity of microcalcifications: Digital systems provide the ability to enhance contrast. Digital systems have the propensity to enlarge structures to the size of the pixel which would result in some distortion of shape. The microcalcifications visible on screen film mammography are usually 250 microns in size or greater so that several pixels would be involved in the display of any visible microcalcification even if 100 micron pixel systems were used.

Display devices are currently not optimal for digital mammography and provide a confounding factor in evaluating the quality of current digital mammography: Printers for digital mammography are still not optimal. In the system we used scan lines are visible and interfere with the determination of shape. Soft copy display systems with adequate brightness are still limited to 2 x 2.5 K display (equivalent to a 100 micron pixel when displaying the whole breast) and optimal image processing parameters for display are not known..

One would therefore assume if one is interested in detecting microcalcifications (as is important in screening mammography) that one might find digital mammography better if indeed the conspicuity of microcalcifications is increased, but that screen film mammography would prove better in diagnostic mammography.

The subjective impression of this relationship, however, is not an absolute statement. If it is difficult to see microcalcifications when they are of low contrast, it is more difficult to determine their shape and to count the very small calcifications. The experiments reported here were performed to determine, with existing 100μ pixel equipment for digital mammography, what the balance is between this tradeoff: low contrast higher resolution of screen film mammography vs. higher contrast lower resolution of digital mammography.

Experimental methods

Equipment

Screen Film System: Fuji IM fine screens, Fuji IM mammographic film.

Digital System: Fuji HR-V imaging plates. Fuji 9000 image plate reader.

Image processing: individually optimized parameter settings, using Fuji standard image processing algorithm, .

Mammographic machine: GE/CGR 600T or 500T, using nominal 0.3 mm focal spot. Phototimed.

Printer: Fuji LP414 laser printer

Certification: Screen Film Mammographic facility is American College of Radiology certified.

Readers: Four Board Certified Diagnostic Radiologists each meeting American College of Radiology requirements as mammography interpreters. Three of the readers have experience with the appearance of digital mammography. One has previously seen only screen film mammography.

Clinical Cases: Random selection of 10 from 30 biopsy proven cancer cases. Random selection of 10 from 100 biopsy proven benign cases. Each case provided with screen film biopsy specimen radiograph. Each image masked so that only region of microcalcifications is shown. Each case was originally detected on screen film mammography and was considered suspicious for cancer following diagnostic evaluation which would have included magnification radiographs. The magnification radiographs were not provided to the radiologists.

Size of microcalcifications measured on cases used:

In each case the smallest and largest microcalcifications visible with the 2 X hand held magnifier were measured using an 8 X magnifier with a measuring reticle allowing measurements from 100μ-2500μ. If a smaller microcalcification could be seen only with the 8 x magnifier, it was not recorded.

Measurements on the biopsy specimens represent the range of microcalcifications visible with the 8 x magnifier. In 9 of the 20 cases, the specimen radiograph was obtained with magnification. Smaller calcifications could be detected in those cases that were magnified.

	Cancer				**Benign**			
Measurements in microns								
	Minimum size		Maximum size		Minimum size		Maximum size	
	AVE	range min	AVE	max range	AVE	range	AVE	range
SF	265	150-450	760	300-2500	265	200-400	1265	400-6000
CR	285	200-400	780	400-5000	285	250-400	1185	300-2500
Biop	156	50-300	783	250-2500	198	75-400	1635	200-6500

From this data one can see that the average size of the smallest microcalcifications in the benign and malignant cases were the same. There was one case of cancer with a 150 micron calcification visible on the screen film mammogram, otherwise the smallest calcifications visible on mammograms in both cancer and non-cancer cases measured 200μ.

On the CR and SF mammograms, at attempt was made to measure the same microcalcifications. The CR mammographic method slightly increases the measurable size of the microcalcifications. This may be an effect of the printer scan lines.

Case presentation: Each case was presented to the radiologists with the specimen radiograph, screen film and digital images. Left-right position of the screen film and digital images randomized. Original screen film mammogram provided. Hand held 2 power magnifier provided.

Questionnaire: Preference between screen film and digital for conspicuity of calcifications, shape of microcalcifications and number of microcalcifications. Is the level of suspicion from the screen film image low or high? From the digital image low or high? Based on all information, do you think the microcalcifications represent benign or malignant disease. Two of the radiologists said all cases were suspicious since all had gone to biopsy and refused to make these assessment in at least some of the cases.

Results

Conspicuity of microcalcifications

Radiologist	All			Cancer Cases			Benign		
	CR	SF	Equal	CR	SF	Equal	CR	SF	Equal
1	10	1	9	5	1	4	5	0	5
2	10	3	7	5	2	3	5	1	4
3	12	6	2	7	3	0	5	3	2
4	5	6	9	3	3	4	2	3	5
Sums	37	16	27	20	9	11	17	7	16

This shows a clear preference for the conspicuity of microcalcification on the digital images. Three of the four radiologists preferred it.

Shape of microcalcifications

Radiologist	All			Cancer Cases			Benign		
	CR	SF	Equal	CR	SF	Equal	CR	SF	Equal
1	8	2	10	4	2	4	4	0	6
2	0	12	8	0	6	4	0	6	4
3	4	5	11	2	3	5	2	2	6
4	0	7	13	0	3	7	0	4	6
Sums	12	26	42	6	14	20	6	12	22

This shows a mixed result of the interpreters of the shape of microcalcifications. Two favored screen film, one favor digital and one was balanced between the two methods.

Number of microcalcifications

Radiologist	All			Cancer Cases			Benign		
	CR	SF	Equal	CR	SF	Equal	CR	SF	Equal
1	6	2	12	3	2	5	3	0	7
2	5	12	3	3	6	1	2	6	2
3	7	7	6	3	4	3	4	4	2
4	3	7	6	0	7	3	2	4	4
Sums	21	28	27	9	19	12	11	14	15

This shows a mixed result of the interpreters of the number of microcalcifications. Two favored screen film, one favor digital and one was balanced between the two methods.

Screen film image
Suspicion of cancer

Radiologist	Cases with cancer			Benign Cases		
	Low	high	no response	Low	High	No response
1	4	6		5	5	
2	3	7		5	5	
3.	5	5		8	2	
4	0	5	5	0	7	3
Sums	12	23	5	13	19	3

This shows that the screen film images did not allow one to accurately choose between benign and malignant cases.

CR image
Suspicion of cancer

Radiologist	Cases with cancer			Benign Cases		
	Low	high	no response	Low	High	No response
1.	3	7		4	6	
2.	5	5		6	4	
3	4	6		8	2	
4	3	3	4	3	4	3
Sums	15	21	4	21	16	3

This shows that the digital images did not allow one to accurately choose between benign and malignant cases. The radiologists did slightly better in defining true negatives on the digital images in this small series, but this is more likely a random rather than a significant difference.

Final Conclusion
Malignant vs. Benign

Radiologist	Cancer Cases			Benign Cases		
	TP	FN	NR	TP	FN	NR
1.	7	3		5	5	
2.	7	3		5	5	
3	3	4	3	4	2	4
4			10		1	9
Sums	17	10	13	14	13	13

This shows that the radiologists could not distinguish between benign and malignant cases in this series.

Discussion

The preference opinions of the Radiologists do not allow clear summary conclusion. Three of the four radiologists prefer the conspicuity of microcalcifications on digital mammography. The fourth considered it equivalent. This may indicate the desirability of digital mammography in breast cancer screening.

Two of the four radiologists clearly consider that screen-film provides better information about shape and number of calcifications. One of the radiologists clearly preferred digital images for shape and number. The fourth radiologist considered screen film and digital images preferred in similar numbers of patients. These findings could mean that screen film is better for shape and counting of calcifications or that greater familiarity with digital images equalizes the preference between screen film and digital. It could also mean, that given a close call between two systems, the familiar appearance is preferred. All four of the radiologists considered the decision of preference in most of these cases difficult to determine.

The Radiologist who considered digital mammography better for delineation of shape and number of calcifications performed at the same level of accuracy for the classification into benign and malignant as two of other radiologists. The radiologist who clearly preferred the screen film images for all purposes felt that all the images were suspicious and refused to choose in most cases between benign and malignant. Thus preference for one system did not affect diagnostic accuracy of the radiologists.

There is the possibility that the case sample we used was too difficult for the test we wished to perform. Since all of these patients were considered sufficiently suspicious to go to biopsy, it may be that the inclusion of cases that were selected at the time of diagnostic mammography not to go to biopsy should have been included as well since the task of the radiologist is to determine whether or not biopsy is indicated. That task, however, is usually decided at the time of diagnostic mammography at which time magnification views are obtained. Such a dataset would, however, remain somewhat unproven since in situ carcinoma can remain quiescent for many years and thus there would always remain some uncertainty about the benign nature of those cases.

We know that there are limitations in the laser printing for digital mammograms at present. A better laser printer may result in slightly better digital images.

In this study, we used masking to identify the location of the microcalcifications. This was to be certain that the radiologists would be able to locate these sometimes very subtle findings. Because of the improved conspicuity found with the digital system, some of the cases might have been detected by the radiologists on the digital mammograms, but not on conventional mammograms. This would affect the clinical accuracy of the overall results.

The results of our ROC study which will use radiologists from outside the institution will be important in determining the clinical meaning of these differences. We intend to test additional patients who, at diagnostic mammography were classified as having benign disease. Most important will be the performance of a screening trial of this digital mammography system.

Summary

A series of 10 breast cancer cases and 10 benign biopsy proved cases were selected using randomization methods from a larger prospectively obtained series. Screen film and 100 micron pixel storage phosphor images were compared using the specimen radiograph as the representation of truth. Four radiologists were asked to indicate preferences. Excluding those cases for which the radiologists considered screen film and digital mammogram images equal, three of the four preferred digital mammography conspicuity, two of three preferred screen film for shape and number of microcalcifications, one preferred the digital image, and the fourth had almost equally divided preference between screen film and digital mammography for shape and number of microcalcifications. Whichever system the radiologists preferred, they failed to be able to distinguish benign and malignant cases in this randomly selected series. This suggests that the subtle differences the radiologists saw between these systems in the evaluation of shape and number may not be clinically significant.

The preference results are considered sufficiently close that an ROC study will be necessary to determine their clinical significance.

Bibliography

Brettle DS, Ward SC, Parkin GJS, et al. A clinical comparison between conventional and digital mammography utilizing computed radiography. British J of Radiology 1994; 67:464-468.

Egan RL, McSweeeney MB, Sewell CW. Intramammary calcifications without an associated mass in benign and malignant diseases. Radiology, 1980. 137:1-7.

Freedman M, Pe E, Nelson M, Lo S-C B, Mun S K: Digital Mammography: Demonstration of a Method of Achieving Adequate Resolution on a Storage Phosphor System. CAR 93, 7th International Symposium Berlin (June 24-26, 1993); 783pp.

Freedman M, Pe E, Zuurbier R, Katial R, Jafroudi H, Nelson M, Lo S-C B, Mun S K: Image Processing in Digital Mammography. SPIE: Medical Imaging, Vol. 2164 (1994); 537-554pp.

Freedman MT, Steller D, Jafroudi H, Lo SCB, Zuurbier RA,Katial R, Hayes W, Wu YC, Lin JS, Steinman R, Tohme WG, Mun SK. Digital Mammography: tradeoffs between 50- and 100-micron pixel size. SPIE Medical Imaging 1995. Paper 2432-09.

Millis RM, Davis R, Stacey AJ. The detection and significance of calcifications int he breast: a radiological and pathological study. British J of Radiology, 1976. 49:12-26

Oestmann JW, Kopans D, Hall DA, et al. A clinical comparison of digitized storage phosphors and conventional mammography in the detection of malignant microcalcifications. Invest Radiol 1988:725-728.

Powell RW, McSweeney MB, Wilson CE. X-ray calcifications as the only basis for breast biopsy. Annals Surgery 1983. 197:555-559.

Sickles EA. Further experience with microfocal spot magnification mammography in the assessment of clustered breast microcalcifications. Radiology 1980; 137:9-14.

Sickles EA. Microfocal spot magnification mammography using xeroradiographic and screen film recording systems. Radiology 1979; 131:599-607.

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DIGITAL MAMMOGRAPHY

Presentation for the Food and Drug Administration
Panel on Digital Mammography
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Conflict of Interest Statement: We are working with the following companies that have or are developing digital radiography systems that could be used for digital mammography. Fuji Photo Film Corporation, 3-M, Prime-X.

EXECUTIVE SUMMARY

Digital mammography is the outgrowth of the convergence of two different paths represented by the progressive improvement of conventional screen film mammography and the progressive improvement of digital projection radiography. The improvements in conventional mammography have been directed towards improvements in contrast and thereby improvements in the conspicuity of normal and abnormal tissues within the breast. Digital mammography represents an extension of trends already evident in conventional mammography towards higher contrast images and higher lesion conspicuity. Radiologic diagnosis done on digital mammograms uses the same signs for the detection of breast cancer as conventional mammography, but appears to show the findings with greater conspicuity and perhaps at a slightly smaller size.

Digital mammography, as with all digital imaging, does require additional clinical training to understand both the value and limitations of computer processing, the artifacts that can be produced and the ways in which computer processing can hide disease. In a fundamental sense, this is no different than learning about conventional screen film mammography, its values and limitations, its artifacts, and the ways in which a badly exposed, handled or processed film can obscure disease.

Digital mammography does require additional quality control procedures to assure that image quality is preserved and artifacts are limited. I believe these must be machine specific and we have devised them for the machine we use.

Digital mammography (using the equipment we use and used with very high standards of quality assurance), does provide, we believe, a small but finite improvement in the conspicuity of the signs of breast cancer. The improvement is so slight that we do not believe that the system we use will improve the accuracy of mammographic detection or classification of lesions that might be due to breast cancer when those mammograms are interpreted by radiologists who are highly skilled in the mammographic detection of breast cancer. Conversely, we believe that the quality of digital mammography performed with this system is equivalent in accuracy to conventional mammography and because of the improvements in lesion conspicuity may improve the accuracy of less skilled radiologists or non-physicians providing initial screening of mammography images prior to their review by a radiologist. This is an hypothesis that we intend to test within the next 6 to 12 months.

On the near horizon, there are systems being developed that may provide a slight additional increment in image quality and it is important that their development not be discouraged by over-regulation. One wishes to do no harm to patients, but harm can occur both by delaying the introduction of an appropriate new technology and by the inappropriate introduction of technology that replaces a proven test. Digital mammography systems are complex and if improperly designed or used can produce the appearance of lesions that could be misinterpreted as signs of breast cancer or hide the findings of breast cancer. Therefore I would recommend that the design of the regulations

(1) Accommodates the progressive quality improvement that will occur as these machines improve over the next few years.

(2) Recognizes the need for tests in geometric test objects, but realizes that different test objects provide different information and that no test object truly reflects the composition of breast tissue or the mammographic signs of breast cancer.

(3) Discusses controls on x-ray exposure.

(4) Includes limited clinical trials without outcome studies, but insists that

(a) these trials include a reasonable sample of breast cancers less than 1 cm in size

(b) includes breasts of different parenchymal patterns

(c) requires a consistency of image processing between images made of geometric test objects and of the breast

(5) Includes clearly defined requirements that the manufacturer supply manuals for machine specific specialty training and machine specific quality control procedures.

INTRODUCTION

THE DEVELOPMENT TRENDS IN CONVENTIONAL SCREEN FILM MAMMOGRAPHY

Conventional screen film mammography has changed dramatically over the past 25 years with improved understanding of how to achieve in a single image the greatest visibility of the signs of small cancers. These trends have been towards the production of high contrast images, with adequate spatial resolution obtained at a radiation dose as low as reasonably achievable (ALARA). The exacting demands of conventional mammography have led to developments of progressively higher contrast screen film combinations, improvements in methods for film processing, and improvements in x-ray mammography machines. Mammography machine development led to dedicated mammography machines with small focal spot sizes, low KVP output, special targets and filters, improvements in breast compression, improvements in scatter rejection (by use of a grid), and the use of phototimers to assure adequate exposure. Although the name "mammogram" has not changed over these 25 years, the method of producing a mammogram and the appearance of the mammographic image are vastly different now than they were before.

THE DEVELOPMENT TRENDS IN DIGITAL PROJECTION RADIOGRAPHY

Digital projection radiography was clinically introduced approximately 15 years ago for applications in bedside chest radiography and has evolved since then towards machines that can perform all projection examinations (such as chest radiographs, abdominal radiographs, musculoskeletal radiographs, mammography, etc) previously obtained with conventional screen film projection radiography. Digital projection radiography has been successful and accepted by many radiologists throughout the world because it provides excellent control of the optical density of the final image resulting in a more consistent appearance of the resulting radiograph. It provides a robustness to the imaging process so that variations in exposure, KVP and patient size produce very little change in final image appearance. It provides this consistency by (1) providing an image receptor that can accept a much larger range of exposures than screen film receptors and (2) by using computer based image processing to correct for some of the changes resulting from mis-exposure. Digital projection mammography is in clinical use in (at least) Japan, England, Switzerland and Denmark. (Brettle, Voegeli, Bidstrup)

Image Processing

Most of the computer based image processing methods used by digital projection radiography are computer implementations of the analog processes used to affect screen film image appearance. The first digital projection radiography machines were developed by the research laboratory of a major x-ray film company. When the digital radiography devices were first designed, the developers decided to make the computer based performance of these system mimic through computer algorithms the best features of the screen film system.

The analogies are :

(1) Use of an appropriate film characteristic curve to affect contrast ~ computer based changes in the look up table to affect contrast.

(2) Use of extended film processing to increase contrast ~ use of an appropriate look up table.

(3) Choice of screen film combination to reduce visible noise ~ computer based noise filtering.

(4) Selection of a lower or higher resolution screen film combination ~ selection of a detector of appropriate inherent resolution.

(5) Use of a bright light to see darker regions of an image ~ (a) use of different window levels to bring the optical density of an image into a range that would not require the use of a bright light combined with the printing of two different images or (b) the use of histogram equalization to balance the optical densities within an image so that a bright light is not needed.

(6) The use of a hand held magnifier ~ electronic zoom to enlarge an image.

(7) Edge emphasis of Xeromammography$^{(R)}$ ~ electronic unsharp masking.

THE BASIS OF IMAGE QUALITY IMPROVEMENT IN DIGITAL RADIOGRAPHY

The important difference between digital radiography and conventional screen film radiography is the separation of three functions of image formation: acquisition of the image data, processing, and display. The film with its chemical processing incorporates all three functions and while radiologists can change the character of each component of this image formation through the implementation of changes in film, screens, developer chemistry, processing temperature and processing time, these changes must be made prospectively, prior to the mammographic exposure and prior to having knowledge of the tissue composition of an individual woman's breast. The main advantage of digital mammography is that these changes can be made after the image data has been acquired allowing the radiologist to adjust image appearance to be patient specific. The best image appearance for a fatty breast is different than that for a dense breast. The electronic adjustment in image appearance can be done automatically by the computer or manually by the technologist or radiologist. In addition, certain of the desired changes in image processing are difficult to accomplish in chemistry based systems and are easier to accomplish with computer algorithms.

NEWER HARDWARE DEVELOPMENTS IN DIGITAL RADIOGRAPHY

Image Acquisition

The initial implementation of digital projection radiography was done using imaging plates that were sensitive to x-radiation and could store the information for later retrieval: they used storage phosphor methodology. The imaging plate stores the information in analog form, but it is extracted and converted into digital form. There are other methods of recording x-ray data in digital form or converting it from analog to digital form. These include film digitization, charge coupled devices (CCD), and other direct x-ray detectors not based on phosphors. Because CCDs are not themselves good detectors of x-radiation, they use a phosphor or cesium iodide layer to convert the x-ray photons into light which is then in turn transferred to the CCD chip directly or through a fiber optic or lens linkage. Most systems depend on the use of a phosphor, either identical or quite similar to the phosphors used in radiographic screens. Cesium iodide is commonly used in the image intensifier tubes of fluoroscopes.

While each of these methods is separate in its engineering methodology and would require different quality control methodologies for manufacture and clinical use, the final images should look quite similar and be of similar clinical value. The methods of machine operation, types of artifacts and image appearance may differ slightly between systems, and thus machine specific training would be desirable. Proper exposure factors for these different devices may differ and should be individually evaluated.

Image Display

Image display is usually done by printing the digital data on laser cameras, the same equipment used for printing CT and MR images. Soft copy displays for digital mammography interpretation are under development.

THE RADIOGRAPHIC SIGNS OF BREAST CANCER

In conventional mammography, the radiographic signs of potential breast cancer are (1) clusters of 5 or more microcalcifications of appropriate size and shape, (2) a mass, which may or may not have a spiculated edge, (3) architectural distortion and (4) certain types of increased tissue since a prior exam. The digital mammographic signs of breast cancer are identical. Digital mammography is not used to find new signs of breast cancer, it uses the conventional signs, but because it can provide a higher contrast image it may increase the conspicuousness of a lesion making it easier for the radiologist to see it. To date, however, there is no study that shows that digital mammography is better than conventional mammography. There is at least a single study (Brettle) where the statistics support the conclusion that digital and conventional mammography are equal. We, at Georgetown are currently at the mid point in data collection for a study with the goal of confirming Brettle's study.

THE EVIDENCE SUPPORTING THE EVENTUAL CLINICAL UTILITY OF DIGITAL MAMMOGRAPHY

The evaluation of new radiologic devices that are evolving from existing devices is usually based on the evaluation of images of geometric test objects comparing the old and new systems, followed by clinical studies based on the comparison of clinical images produced by the old and new systems. When the signs of disease are well known and the changes made in the new image reflect past trends in image improvement, full scale outcome studies are rarely done and would probably represent a waste of resources. One does not do an outcome study for each new conventional screen film combination used for mammography. In conventional mammography, there is a general consensus of what images should look like and how to differentiate a good from a bad image. The signs of breast cancer on mammograms are well understood, but radiologists would like to able to see these signs of breast cancer more easily and with better definition. If digital mammography could improve the conspicuity of the accepted mammographic signs of breast cancer and especially if it could demonstrate better the signs that help radiologists distinguish benign from malignant, it would and should replace conventional mammography. Digital mammography is not yet at this level of quality, but it is close.

There is evidence in geometric test objects that digital mammography can equal or slightly exceed conventional screen film mammography in the conspicuity of the details in geometric test objects. The following chart represents data we have presented on our findings in several geometric test objects. (Freedman, 1995)

TABLE OF SMALLEST OBJECT SEEN: SCREEN FILM VS DIRECT DIGITAL 50 AND 100 μ SYSTEMS

Test Object	Screen Film	100 micron phosphor	50 micron CCD
CDMAM	130. 100 at 5x mag	100 at 1 micron thick	100 at 0.8 microns thick
CIRS Detail	240	160	160
RMI 156	240 (3/6)	240 (3/6))	240 (3/6)
CIRS Half Round	160	160	160

(CDMAM test object from Nuclear Associates, Carle Place, New York; CIRS, Norfolk Virginia. Fuji (Tokyo) Kyokko UM Fine Screen with Fuji UM-MA-HC film. The 100 micron device is a whole breast storage phosphor machine. The 50 micron CCD is a digital spot device.)

There are slight improvements in the visibility of smaller object details in some of the test objects with the digital methods. Recent work by Roehrig confirms the slight advantage of a 50 micron CCD system over screen film mammography in tests using the CDMAM test object. (Krupinski, Roehrig)

When one looks at the images of these test objects, it is quite clear that while the conventional and digital systems performed similarly in the detectability of small objects, the contrast of the details is visibly higher in the digital images. If you combined the Georgetown data with Roehrig's data, together we have tested 3 different digital systems with essentially the same findings.

The improvement in object conspicuity in small breast cancers is also easily seen in the cases I am showing at this meeting. In these cases, obtained with the approval of the Georgetown Institutional Review Board and with signed patient consent, we obtained whole breast digital mammograms in woman whose conventional mammogram indicated the need for breast biopsy. A side by side comparison shows the improved conspicuity of the cancers. This series includes a five mm ductal carcinoma in situ, a six mm invasive ductal carcinoma, and a multicentric carcinoma with the largest focus 8 mm and invasive. We currently have 63 cases in our clinical trial each with a complete conventional mammogram and a digital mammogram with one view of each breast. Each of these patients has had a biopsy, and when

open biopsy was performed, a specimen radiograph was obtained. Our current experimental design, does not allow us to test scientifically whether or not digital mammography will detect cancers that conventional mammography misses.

WHAT RADIOLOGISTS WOULD LIKE TO SEE IN IMAGES RESULTING FROM A NEW MAMMOGRAPHIC SYSTEM

I believe if you offered to practicing clinical radiologists the ability to have breast images (conventional or digital) that contained any of the following changes, that radiologists would prefer them to current mammography and consider them likely to improve detection or classification.

(1) Improved conspicuity of microcalcifications and small masses.

(2) Improved definition of the shape of microcalcifications.

(3) Improved definition of the appearance of the edge of small masses.

(4) Improved conspicuity of architectural distortion.

(5) The ability to interpret accurately more mammograms per day.

(6) Direct magnification or zooming to eliminate the need to use a magnifying glass.

There is the potential for digital mammography to do each of these if the trends in digital mammography already demonstrated continue.

QUALITY CONTROL ISSUES

Digital systems and conventional systems can both produce artifacts that mimic or, conversely, obscure the signs of cancer. Both systems can create calcium like and mass like artifacts or obscure true findings. Quality control procedures for digital systems overlap procedures needed for screen film systems and also impose additional quality control requirements. There are sufficient differences between digital systems, that one cannot describe the quality control requirements for all systems directly, but one can indicate what should be in such procedure manuals.

1. If the digital system can produce artifacts that can be misinterpreted as microcalcifications, training should be provided in how to decrease or avoid such artifacts and how to recognize them when they occur.

2. If the digital system can produce artifacts that can be misinterpreted as small masses, training should be provided in how to decrease or avoid such artifacts and how to recognize them when they occur.

3. If the image processing can be adjusted to obscure small masses or microcalcifications, training should be provided in how to decrease or avoid such artifacts and how to recognize them when they occur.

4. If the image processing can be adjusted to produce small masses or microcalcifications, training should be provided in how to decrease or avoid such artifacts and how to recognize them when they occur.

5. If under or over exposure of the breast can occur and be obscured by the image processing of the system, it would be preferable to redesign the machine to avoid such possibility. Should that not be possible, training should be provided in how to decrease or avoid such under or over exposure and how to recognize it should it occur.

PIXEL SIZE

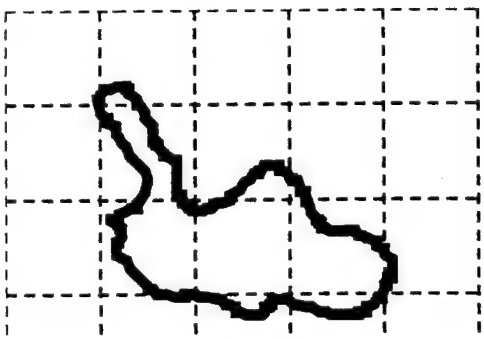
Pixel size affects resolution, the detection of small objects, the evaluation of shape of small objects, the exposure required for digital mammography, and the machine and data handling costs of the machines. The larger the pixel, the less the data handling costs, (in general) the less the required radiation, the lower the visibility of shape and edges and the lower the visibility of noise in the image.

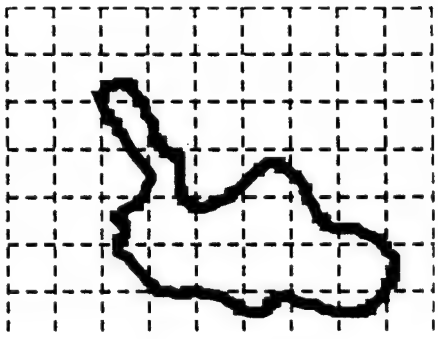
PIXEL SIZE AND SMALLEST DETECTABLE OBJECT

Given the importance that pixel size has in each of these factors which affect the quality of a mammogram, one would anticipate that there would be much written material on this topic. There are surprisingly few scientific studies of this question: Articles in the late 1980s by HP Chan suggested that 100 micron digitized film was not adequate for the detection of the smallest microcalcifications seen on screen film mammography and work by Oestmann suggested that with storage phosphor technology 100 micron pixels could, in a test object, detect all the calcification clusters seen on screen film mammography systems, but not each individual microcalcification. Last week, I presented at the SPIE Medical Imaging Conference our data that suggested that the improvements in the use of a 50 micron vs a 100 micron pixel were (1) slight improvements in the contrast of detected objects and (2) a small improvement in the definition of the shape of objects. We did not see any decrease in the minimal size of objects seen, probably because this effect is slight and our available test objects did not have small enough decrements in size to allow this effect to be detected. A slight decrease in detectable object size would be expected, however. In geometric test objects, images made with a 100 micron pixel show objects equal to or slightly smaller than screen film images, depending on the test object. (See Table 1.)

PIXEL SIZE AND OBJECT SHAPE

Shape determination is related to pixel size. The more pixels contained within the shadow of the object, the more accurately its shape will be depicted.





At the moment, our data, which needs independent confirmation, suggests that the improvement that results from the use of a 50 micron pixel is finite, but real when comparison is made to screen film and 100 micron pixel mammography. Because the improvement in shape definition is slight, it is unclear what effect this will have on the detection of breast cancer by a human observer. There is data that shows that detection accuracy in computer aided diagnosis algorithms is improved by the use of digitized film pixels sizes of 25, 35, and 50 microns compared to pixels sizes of approximately 100 microns. (HP Chan, H. Fujita).

RESOLUTION VS DETECTION

Pixel size is related to resolution: the ability to separate two adjacent objects. Detection is related to object contrast, the amount of noise in the background and the variability of the background. Object contrast is related to pixel size. If an object is of high enough contrast, it can be detected even if it is smaller than a single pixel. This is analogous to the partial volume effect of seen in other digital imaging systems.

GEOMETRIC TEST OBJECTS

Problems with the use of standard test objects:

(1) The RMI 156 test object is a quality control phantom, not a performance test for imaging systems.

(2) The testing of digital radiography systems with standard test objects is valuable, but because these do not represent the true tissue patterns in the breast, the findings on these test objects should not be considered definitive measure of image quality, especially if one is comparing the functioning of two different machines.

(3) Usual measurements of resolution of conventional screen film mammography measure high contrast resolution. The resolution of screen film systems, however, falls with decreasing contrast of the image. The findings of breast cancer are all relatively low contrast findings and thus it is low contrast resolution that is important the evaluation of systems for mammography. There is little difference in the low contrast resolution of conventional screen film and digital systems combined with appropriate image processing.

(4) Image processing can enhance the low contrast resolution in digital systems, enhancing the contrast of low contrast objects and improving their conspicuity. Geometric test objects can be manufactured to include diffuse structural features meant to simulate breast tissue pattern. These do not reflect the structural characteristics of the breast, but this test object structural noise can be enhanced by image processing to produce a bizarre image quite different from what the same image processing produces in the human breast.

Because of these problems, I believe that one should test several different test objects in comparing digital and conventional mammography. These test objects should be commercially available so that the measurements can be reproduced at another site. Because image processing can result in images of test objects that are very good, but produce images of the breast that are uninterpretable, the same image processing settings used for demonstration of test objects should be used in processing the clinical breast images in any trial. Because increases in exposure in digital systems improve the image appearance of geometric test objects, exposures used in the test objects and in patients should be recorded and be comparable between screen film and digital systems, unless the digital system can be shown to have better performance that is likely to be clinically significant and sufficient to justify the increased patient dose.

We have found in our tests, that digital mammography with a 100 micron pixel, nominal 5 line pair resolution, with appropriate image processing, most likely (but not yet statistically proven) provides equal or slightly better conspicuity of lesions than screen film mammography. Parkin's statistical data supports a conclusion of the performance being equal. We believe that there are definite advantages to the use of a 50 micron system if one intends to use computer aided diagnosis algorithms. It is likely based on work in geometric test objects, but not proven in the breast in vivo, that a 50 micron pixel will provide increased object contrast and thereby improve object conspicuity. We are, however, unaware of any clinical evidence that digital mammography with a 50 or a 100 micron pixel would improve breast cancer detection.

EXPOSURE

Decreased Exposure

Early reports on digital mammography suggested that the exposure to patients might be reduced by the use of digital mammography methods. This is a complex issue since the 100 micron digital system we use does perform better than screen film systems at lower exposures; It is not, however, functioning with its maximal quality at these lower exposures. The machine we have used experimentally does provide conspicuity equal to screen film mammography at the usual screen film dose and appears to perform slightly better than conventional mammography at a still higher dose.

Because our tested 100 micron system does perform better than screen film mammography at low exposures as shown in geometric test objects, is seems likely that digital systems would provide better detection of small objects in areas of increased breast radiodensity if the comparison screen film mammogram was underexposed in the same region. We would not expect to see an advantage if the region in question were properly exposed. Below is a chart from our recent paper on this topic (Freedman, 1995).

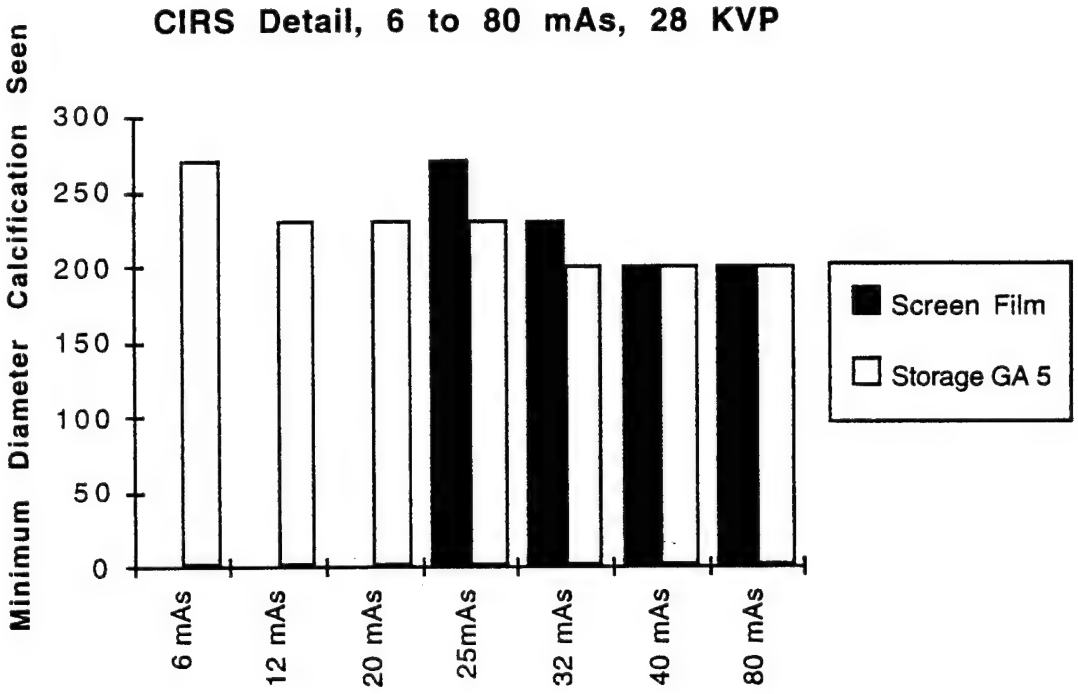


Figure 1. This chart demonstrates that at mAs less than 25, while the storage phosphor system could demonstrate objects, the screen film failed to demonstrate any of the objects. At 25 and 32 mAs, the storage phosphor demonstrated smaller objects than screen film. At 40, and 80 mAs, the two systems performed equivalently. 40 mAs in this experiment corresponds to a screen film optical density of 0.42. Under these test conditions, the storage phosphor system provided more information at low exposures than did the screen film system. (Fuji (Tokyo) Kyokko UM Fine Screen with Fuji UM-MA-HC film. The 100 micron device is a whole breast storage phosphor machine.) (Storage = Storage Phosphor Radiography. GA = gradient angle of the look up table.) (Freedman, 1995)

Increased Exposure

Some digital systems will show improved small object detectability with exposures greater than those used in conventional screen film mammography. Until and unless this increased exposure can be related to improved detection of breast cancer, it should be avoided.

THE IMPORTANCE OF THE SEARCH FOR BETTER MAMMOGRAPHY

Current screening mammography is an excellent clinical tool. It has a relatively high sensitivity, but is less than ideal because of its relatively low specificity and relatively high cost, particularly if one includes the costs of biopsies resulting from its low specificity. Detection of breast cancer when it is small, improves prognosis as shown by Bedwani.
Figure 2

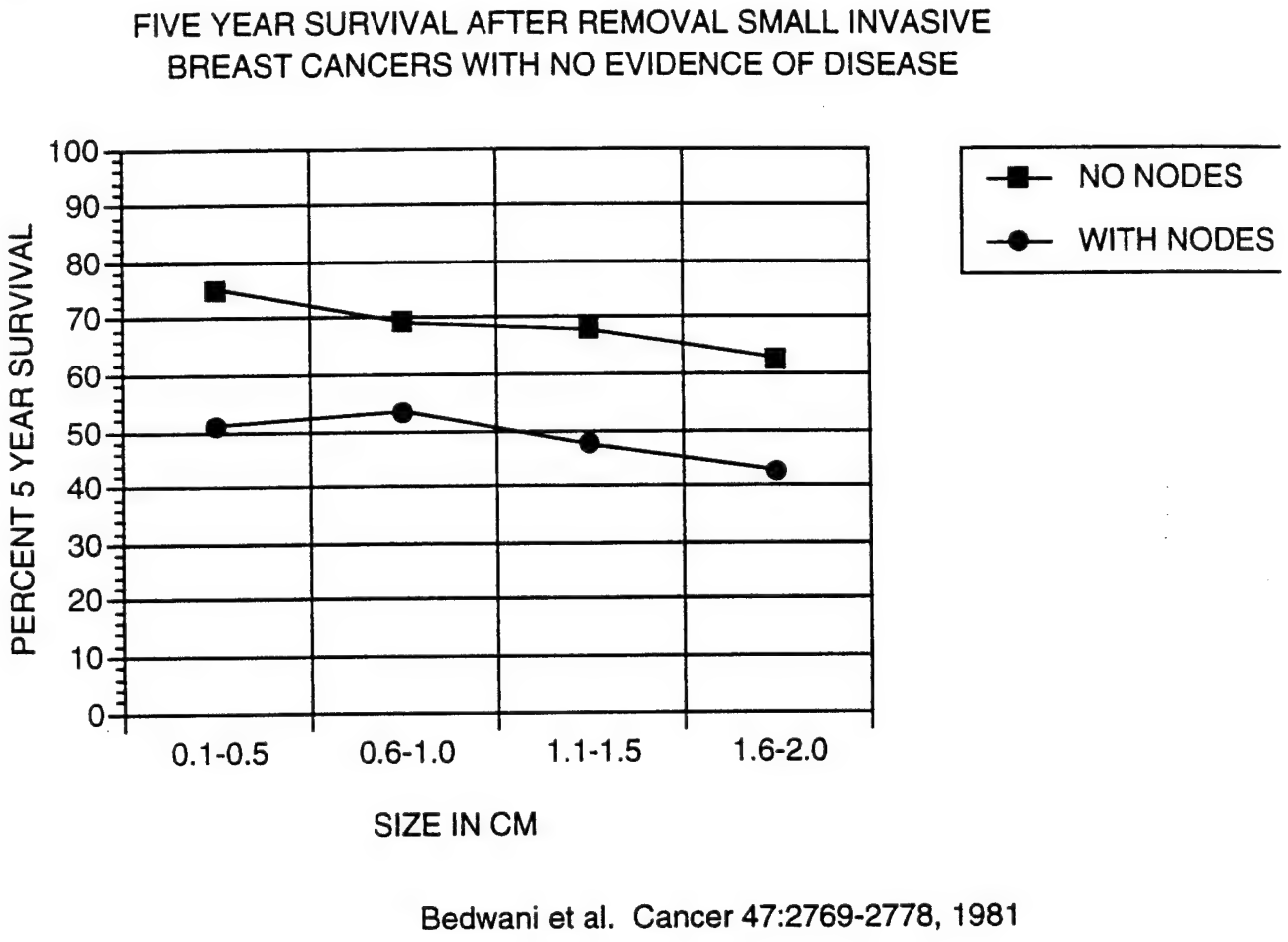
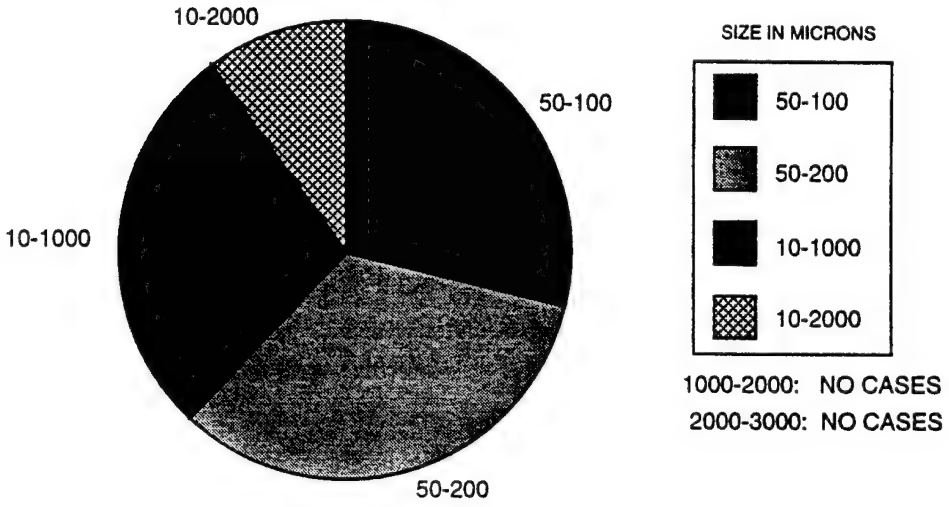


Figure 2. This chart, drawn from Bedwani's data is for patients with small breast cancers that were locally invasive. The size measurement is the size measured by the pathologist. The patients are divided into two groups, those with and without nodal metastases. One can see that the five year disease free survival decreases with increasing size, even for lesions less than one cm in size.

It is also known that breast cancer has smaller microcalcifications that those currently detectable by any imaging method in vivo.. The work of Egan based on analysis of specimen radiographs is one of several papers (Egan, Powell, Millis) supporting this.

SIZES IN MICRONS OF MICROCALCIFICATIONS IN 115 BREAST CANCERS
WITH MICROCALCIFICATIONS AS ONLY SIGN OF CANCER



RL Egan. Radiology 137:1-7, 1980

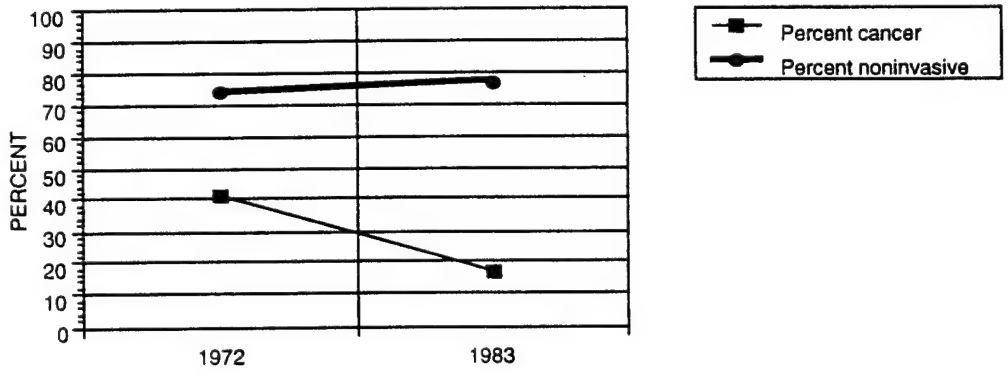
This chart demonstrates the proportion of cases with microcalcifications limited within certain ranges of size. Approximately 28% of cancers had microcalcifications limited to the range of 50-100 μ. A second group had calcifications limited to 50-200 μ. It is these two groups that should show some benefit from improved detectability of microcalcifications.

While there is debate about the size of microcalcifications detectable on conventional screen film screening mammography in vivo, our experience suggests that the minimal detectable size in screening mammograms is in the range of 200-250 microns.

THE POTENTIAL IMPLICATIONS OF FINDING SMALLER LESIONS THAT COULD BE CANCER

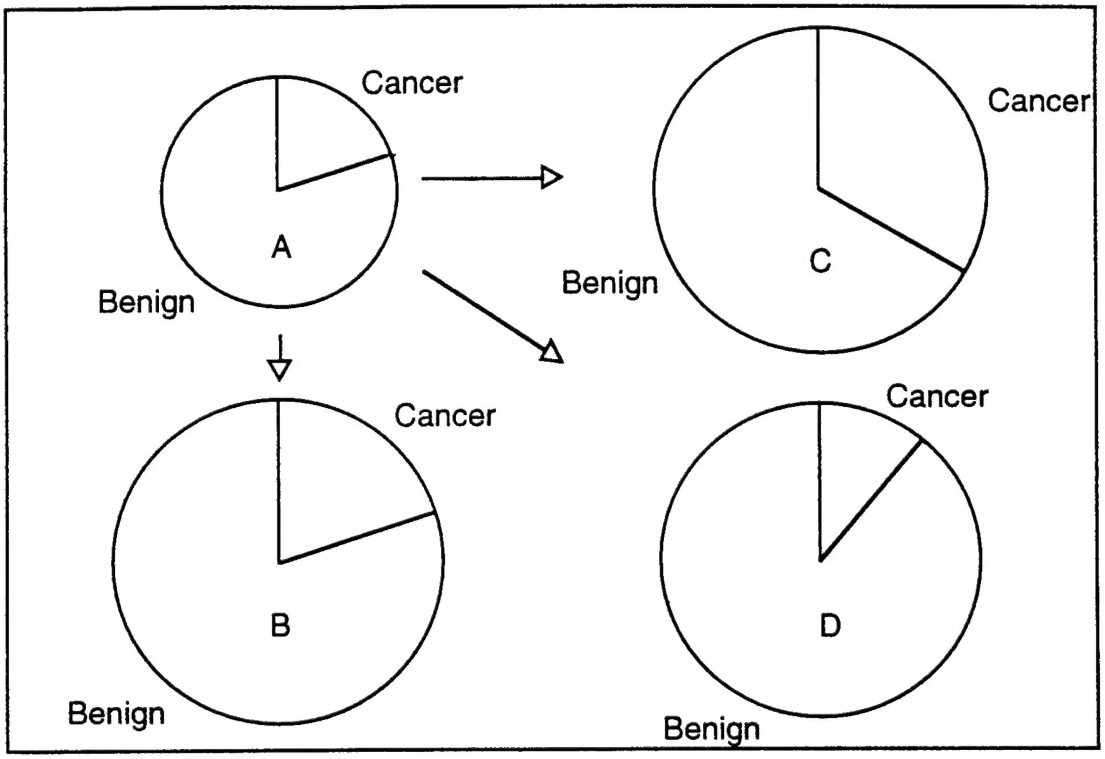
One might be concerned that finding smaller microcalcifications or smaller masses might shift the proportion of such lesions that represent cancer altering the cost of finding cancer through screening. If the proportion of cancers was decreased, this would result in increases in both the psychological and physical trauma of unnecessary breast biopsies. Currently, we do approximately three biopsies of masses or calcifications for each cancer detected. In other centers it can be 1 in 5. In one series, only 17 % of biopsies done for microcalcifications showed cancer (Powell). If one finds smaller microcalcifications and smaller masses, one might find that the frequency of biopsies demonstrating cancer had increased or decreased. I am aware of no data on this issue. The data of Powell shows that from 1972 to 1983, the number ratio of cancers to benign disease detected decreased in patients biopsied for microcalcifications. A recent unpublished series (Smith) shows a 17 percent ratio of cancer in stereotactic biopsy of microcalcification clusters, the same as in Powell's series from 1983. Thus the rate of true positive detections did not change despite substantial improvements in image quality in the interval. This suggests that further improvements in image quality might follow the same trend with an increase in cases detected, but no change in the proportion due to cancer.

BIOPSIES FOR MICROCALCIFICATIONS AS ONLY ABNORMALITY ON MAMMOGRAM



Powell et al. Annals of Surgery 197: 555-559, 1983

As shown in this drawing, there are several potential outcomes should new technology allow the detection of smaller lesions.



In this drawing, let A represent the current detection of microcalcifications and small masses. If we increase the detection rate as shown by the larger circle in B (representing an increase in sensitivity with no change in specificity), then the percentage cancers remain the same and we have not altered the expected cost of detecting cancer. Ideally, as shown in C, we would hope that the better definition of detail would allow us to improve the proportion of cancers detected (an increase in sensitivity and specificity or just an increase in specificity). But, as shown in D, the proportion of cancers might decrease resulting in an increased number of breast biopsies with little or no improvement in the detection of breast cancer (no change in sensitivity, decrease in specificity). Which of these scenarios will occur is unknown.

IMPROVING THE SENSITIVITY OF MAMMOGRAPHY

There is reason to believe that digital mammography will improve the sensitivity of mammography for the detection of breast cancer. Currently, there is however no evidence supporting this. Reasons to believe that digital mammography will result in improvements in beast cancer detection relate to the improved conspicuity of lesions whose mammographic appearances currently are used as indicators of the presence of possible breast cancer. If you improve the conspicuousness of such findings, they are less likely to be missed.

IMPROVING THE SPECIFICITY OF MAMMOGRAPHY THROUGH DIGITAL METHODS

To improve the specificity of mammography, one must attempt to classify lesions that are detected into benign and malignant categories with greater precision than is now possible. The current mammographic findings that are used to somewhat improve this categorization are related to the shape of microcalcifications, their number, the shape of the edges of identified masses and the presence or absence of change from the prior mammogram. Digital mammography at 50 microns, as supported by our preliminary data and not yet independently confirmed, appears to provide slightly greater information about shape to the human observer than conventional screen film mammography. Our data is very preliminary data obtained at the start of a complex project on shape definition. 50 micron data does appear to be important for computer algorithms for breast cancer detection and classification of microcalcifications into benign and malignant categories.

THE IMPORTANCE OF DIGITAL MAMMOGRAPHY FOR THE EVENTUAL CLINICAL IMPLEMENTATION OF COMPUTER AIDED DIAGNOSIS

The use of computer analysis to assist the radiologist in the detection of breast cancer and in the categorization of breast lesions into benign and malignant categories is currently in pre-clinical trial at the University of Chicago. A clinical trial is about to begin at Georgetown. Based on preliminary data, it is likely that computer aided diagnosis will become an important aid to the radiologist. We anticipate that the radiologist will use this computer aid as a second opinion or second reader of the mammogram and also to provide predictive statistics of the chance that a lesion is benign or malignant. Acquiring the mammogram in a direct digital form will make it substantially easier to implement computer aided diagnosis methods into clinical practice. Improved classification of identified lesions into benign and malignant categories should help to prevent some unnecessary biopsies (Wu, Lo, Chan). This computer based improved classification should result in improved specificity of mammographic findings.

DIGITAL MAMMOGRAPHY AND LEAD TIME BIAS

When improvements in digital mammography allow the detection of smaller cancers, the clinical outcome may not really change because of lead time bias. Although extensive future testing and confirmation would be necessary, this lead time effect may allow the interval between screening mammograms to be safely increased without affecting long term outcome. If detecting breast cancer at a smaller size can be done with high sensitivity, but does not affect its long term prognosis, lengthening the interval between screening would have no effect on outcome, but would decrease the cost of breast cancer screening programs proportionately.

DIGITAL MAMMOGRAPHY AND THE COST OF HEALTH CARE

At this time it is not possible to evaluate the long term effect of the introduction of digital mammography on the cost of health care. The initial effect would be increased cost because of the need to acquire new equipment. In the longer view, this initial equipment cost may be offset by the following potential, but, as yet, experimentally unproved benefits: (1) Improved specificity based on better information about shape, decreasing the number of biopsies for benign disease. (2) Detection of cancer at an earlier stage. (3) Use of lead time bias to increase the spacing between screening mammograms. (4) Detection of cancer at an earlier stage in women with dense breasts, especially younger women. Based on preliminary work with computer aided classification of mammographically identified lesions, improved specificity seems likely. Smaller cancers, one would expect, would proportionately be shifted towards those in a lower stage. The recent work on exposure effect differences between conventional screen film and digital mammography (Freedman, 1995) suggests that digital mammography might offer advantages in the dense breast. The contrast enhancement that allows smaller and lower contrast objects to be detected digitally (Freedman, 1995) could benefit the earlier detection of breast cancer in dense breasts. Clearly further research is needed to explore the full potential of digital mammography.

SUMMARY

Digital mammography is the outgrowth of the convergence of two different paths represented by the progressive improvement of conventional screen film mammography and the progressive improvement of digital projection radiography. The improvements in conventional mammography have been directed towards improvements in contrast and thereby improvements in the conspicuity of normal and abnormal tissues within the breast. Digital mammography represents an extension of trends already evident in conventional mammography towards higher contrast images and higher lesion conspicuity. Radiologic diagnosis done on digital mammograms uses the same signs for the detection of breast cancer as conventional mammography, but appears to show the findings with greater conspicuity and perhaps at a slightly smaller size.

Digital mammography, as with all digital imaging, does require additional clinical training to understand both the value and limitations of computer processing, the artifacts that can be produced and the ways in which computer processing can hide disease. In a fundamental sense, this is no different than learning about conventional screen film mammography, its values and limitations, its artifacts, and the ways in which a badly exposed, handled or processed film can obscure disease. Since digital projection imaging is not extensively explored in most radiology residencies, courses would be needed to properly train radiologists in the proper use of digital mammography machines.

Digital mammography does require additional quality control procedures to assure that image quality is preserved and artifacts are limited. I believe these must be machine specific and we have devised them for the machine we use. Physicists, radiologic technologists and service engineers will need training in the specific requirements of the digital mammography machine they will be using.

Digital mammography (using the equipment we use and used with very high standards of quality assurance), does provide, we believe, a small but finite improvement in the conspicuity of the signs of breast cancer. The improvement is so slight that we do not believe that the system we use will improve the accuracy of mammographic detection or classification of lesions that might be due to breast cancer when those mammograms are interpreted by radiologists who are highly skilled in the mammographic detection of breast cancer. Conversely, we believe that the quality of digital mammography performed with this system is equivalent in accuracy to conventional mammography and because of the improvements in lesion conspicuity may improve the accuracy of less skilled radiologists or non-physicians providing initial screening of mammography images prior to their review by a radiologist. This is an hypothesis that we intend to test within the next 6 to 12 months.

On the near horizon, there are systems being developed that may provide a slight additional increment in image quality and it is important that their development not be discouraged by over-regulation. One wishes to do no harm to patients, but harm can occur both by delaying the introduction of an appropriate new technology and by the inappropriate introduction of technology that replaces a proven test. Digital mammography systems are complex and if improperly designed or used can produce the appearance of lesions that could be misinterpreted as signs of breast cancer or hide the findings of breast cancer. Therefore I would recommend that the design of the regulations

(1) Accommodates the progressive quality improvement that will occur as these machines improve over the next few years.

(2) Recognizes the need for tests in geometric test objects, but realizes that different test objects provide different information and that no test object truly reflects the composition of breast tissue or the mammographic signs of breast cancer.

(3) Discusses controls on x-ray exposure.

(4) Includes limited clinical trials without outcome studies, but insists that

(a) these trials include a reasonable sample of breast cancers less than 1 cm in size

(b) includes breasts of different parenchymal patterns

(c) requires a consistency of image processing between images made of geometric test objects and of the breast

(5) Includes clearly defined requirements that the manufacturer supply manuals for machine specific specialty training and machine specific quality control procedures.

BIBLIOGRAPHY

Chan HP. Personal communication regarding effect of pixel size of film digitization on accuracy of computer aided diagnosis, February 27, 1995.

Fujita H, Endo T, Matsubara T, et al. Automated detection of masses and clustered microcalcifications on mammograms. SPIE Medical Imaging, paper # 2434-77. Presented February 27, 1995. In press.

Roehrig H, Krupinski EA, Yu T. Physical and psycho-physical evaluation of digital systems for mammography. SPIE Medical Imaging, paper # 2436-14. Presented February 27, 1995. In press.

Freedman M, Steller D, Jafroudi H, et al. Digital mammography: The effects of decreased exposure. SPIE Medical Imaging, paper # 2432-49. Presented February 27, 1995. In press.

Freedman M, Steller D, Jafroudi H, et al. Digital mammography: Tradeoffs between 50- and 100-micron pixel size. SPIE Medical Imaging, paper # 2432-09. Presented February 27, 1995. In press.

Bedwani R, Vana J, Rosner D, et al. Management and survival of female patients with "minimal" breast cancer. Cancer 47:2769-2778, 1981

Egan RL, McSweeney MB, Sewell CW. Intramammary calcifications without an associated mass in benign and malignant diseases. Radiology, 1980. 137:1-7.

Millis RM, Davis R, Stacey AJ. The detection and significance of calcifications in the breast: a radiological and pathological study. British J of Radiology, 1976. 49:12-26

Powell RW, McSweeney MB, Wilson CE. X-ray calcifications as the only basis for breast biopsy. Annals Surgery 1983. 197:555-559.

Freedman M, Pe E, Nelson M, Lo S-C B, Mun S K: Digital Mammography: Demonstration of a Method of Achieving Adequate Resolution on a Storage Phosphor System. CAR 93, 7th International Symposium, Berlin, Germany (June 24-26, 1993); 783 pp.

Freedman M, Pe E, Zuurbier R, Katial R, Jafroudi H, Nelson M, Lo S-C B, Mun S K: Image Processing in Digital Mammography. SPIE: Medical Imaging, Vol. 2164 (1994); 537-554pp.

Freedman M, Mun S K, Pe E, Lo S-C B, Nelson M: Image Optimization on the Fuji AC-1. SPIE: Medical Imaging (1993). Vol 1897: 480-502.

Chan HP, Vyborny CJ, MacMahon H et al. Digital mammography: ROC studies of the effects of pixel size and unsharp mask filtering on the detection of subtle microcalcifications. Invest Radiol 1987. 22: 581-589.

Maidment AD, Yaffe M, Plewes DB et al. Imaging performance of a prototype scanned-slot digital mammography system. SPIE Medical Imaging 1993. 1986:93-103.

Lo JY, Grisson AT, Floyd CE et al. Computer aided diagnosis of mammograms using an artificial neural network. SPIE Medical Imaging, 1995. Paper 2434-65. In press.

Chan HP, Wei D, Lam K, et al. Computerized detection and classification of microcalcifications on mammograms. SPIE Medical Imaging, 1995. Paper 2434-70. In press.

Smith DV. Written copy of data analysis of results of one year's experience with stereotactic core biopsy. May, 1994.

Oestmann JW, Kopans D, Hall DA, et al. A comparison of digitized storage phosphors and conventional mammography in the detection of malignant microcalcifications. Invest Radiol 1988:725-728.

Wu YC, Lo S-CB, Zuurbier RA, Hasegawa A, Freedman M, Mun SK. Classification of Microcalcifications Using A Hybrid Neural Network. SPIE: Medical Imaging 1994. 2167:630-641

Krupinski EA, Roehrig H, Yu T. Observer performance comparison of digital radiograph systems for stereotactic breast needle biopsy. Academic Radiology 1995. 2:116-122.

Brettle DS, Ward SC, Parkin GJS, et al. A clinical comparison between conventional and digital mammography utilizing computed radiography. British J Radiology 1994: 464-468.

Voegeli E. in Busch HP and Georgi M (Eds) Digital Radiography Workshop. Schnetztor-Verlag GmbH, Konstanz. 1992. p. 90-91

Bidstrup P. in Busch HP and Georgi M (Eds) Digital Radiography Workshop. Schnetztor-Verlag GmbH, Konstanz. 1992. p 16-17.